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"A COMPARATIVE STUDY OF SUB LINGUAL, ORAL AND VAGINAL MISOPROSTOL IN CERVICAL RIPENING FOR FIRST TRIMESTER ABORTION"

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ABBREVIATIONS

MTP- Medical termination of pregnancy

MMA- Medical method of abortion

MA – Medication abortion

MVA – Manual vacuum of aspiration

LMP – Last menstrual period

RMP – Registered medical practitioner

WHO- World health organization

FOGSI- Federation of Obstetrics and Gynaecological Societies of India

D&C- Dilatation and curettage

S/L- Sub lingual

Se- Suction Evacuation

Pg- Prostaglandin

Rcog- Royal College of Obstetricians & Gynecologists

INTRODUCTION

INTRODUCTION

Abortion is defined as termination of pregnancy, either spontaneous or intentional before 20 weeks of gestation or birth weight less than 500 gm [1]. According to WHO, unsafe abortion is responsible for death of 36,000 women annually [57]. Almost one-fifth of worldwide abortions take place in India. In India 12-18% of maternal mortality is attributable to abortions and is mostly caused by illegal abortions [2].

MTP was legalized in India in 1971, and came into effect in 1972[4].One of the main objectives of introducing the Act was to reduce mortality & morbidity due to illegal abortions. The act was amended in the year 2002, and was notified in the gazette in June 2003[6].

Various methods e.g. Medical and surgical are used for MTP. Medical methods include the use of drugs like mifepristone, mifepristone & misoprostol, methotrexate & misoprostol, and tamoxifen & misoprostol. Medical abortion is an excellent non-invasive option for early abortion as it avoids the risk of anaesthesia and surgical trauma to the cervix, uterus and other organs. The disadvantages of medical abortion are that medical supervision and follow up is of utmost importance. It takes a longer time, thus causing prolonged bleeding, which is quite worrisome for the patient. More importantly, medical abortion should be attempted only if the patient has access to 24hour emergency services, which makes it unsuitable for rural areas [16].

Surgical methods for MTP are menstrual regulation, vacuum aspiration [6] [9], suction evacuation, and dilatation & evacuation. D & E is the most commonly performed procedure and is the method of choice in 1st trimester MTP. It is highly effective but since cervical dilatation is an important critical step before D&E hence it is associated with side-effects such as genital tract injury, especially cervical injury in addition to infection, perforation of the uterus or Asherman's syndrome. The future fertility of women who undergo this procedure may be jeopardized. Cervical ripening by mechanical methods or pharmacological agents is beneficial prior to dilatation & evacuation (D&E) as it reduces the risk of cervical injury, uterine perforation, haemorrhage and incomplete uterine evacuation [2] [3]. It also shortens the duration of suction evacuation procedure.

In 1973, first article describing the effect of preoperative cervical dilatation was published [5].The first trial using misoprostol as cervical ripening agent has been published in 1994 [6].

Several drugs are available for cervical ripening. Among them Misoprostol is an important drug used for cervical ripening [7]. It is a prostaglandin E1 analogue which was initially used as a protective agent for gastric ulcer. The advantages of using misoprostol are it is stable at room temperature so does not require refrigeration, it is easily available & relatively economical, it minimises cervical injuries& reduces intra-operative blood loss, it reduces the requirement of anaesthesia and it can be administered via several routes such as sublingual, oral, buccal and vaginal [8]. Hence misoprostol is an ideal agent for pre-abortion cervical ripening. Several studies have shown that vaginal administration is more effective than oral route[9]. Sublingual administration is a relatively new method in which misoprostol tablet is put beneath the tongue and it dissolves within 10-15 minutes [16].

Several studies have been done worldwide to ascertain the ideal route and dosage schedule of misoprostol for cervical ripening but no consensus has been reached. Number of studies in India to compare oral, sublingual, and vaginal misoprostol for cervical ripening is very less. Hence, we carried out a study to compare the effectiveness of vaginal, sublingual and oral misoprostol for cervical ripening before 1st trimester MTP in order to decrease the risk of injury to genital organs and to achieve additional benefits such as reduction in the short and long-term complications, amount of blood loss, pain intensity and duration of surgery, and to improve operative ease for the surgeon [16]. The main parameters compared were degree of dilatation of cervix three hours after administration, duration of time required for SE procedure, blood loss during the procedure and associated side effects.

AIMS

&

OBJECTIVES

AIMS & OBJECTIVES

AIM:

Comparison of sublingual, oral and vaginal Misoprostol (400 microgram) as a cervical ripening agent 4 hours prior to 1st Trimester surgical abortion.

OBJECTIVES:

To compare the efficacy and tolerability of tablet Misoprostol 400mcg as a cervical ripening agent given 4 hours prior to suction evacuation (SE) in 1st Trimester abortion through Sublingual, Oral and Vaginal routes.

PRIMARY OUTCOME:

Measures to assess the efficiency of misoprostol in terms of Cervical Dilatation Achieved, Intra-operative Blood Loss, Operative Time.

SECONDARY OUTCOME:

Measures to assess Acceptability, Patient Satisfaction, Pain Perception and Adverse Effects.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Background

Abortion is the termination of pregnancy by removal or expulsion of fetus or embryo. Abortion which occurs without intervention is known to be miscarriage or spontaneous abortion. when an abortion is done with medicine or medical/surgical procedure it is known as induced abortion. As per WHO (world health organization) report, 19 million women worldwide undergo unsafe abortion each year and 18.5 million of these procedures are carried out in the developing countries[2]. Mortality attributed to unsafe abortion is estimated at about 36000 women each year. The Indian MTP Act permits self-willed termination of pregnancy before the age of fetal viability for well-defined indications. It should be performed by registered medical practitioners in a recognized place approved by the competent authority [57].

METHODSOF ABORTION

MEDICAL METHODS:

1. Mifepristone and Misoprostol
2. Metotrexate and Misoprostol
3. Tamoxifen and Misoprostol
4. Intracervical or Extraovular instillation of cerviprime gel (PGE2)

MECHANICAL METHOD:

1. Foley bulb induction alone or with misoprostol

SURGICAL METHODS:

1. Menstrual regulation
2. Vacuum aspiration
3. Dilatation and Evacuation
4. Suction and Evacuation [57]

MENSTRUAL REGULATION

It is the aspiration of endometrial cavity within 14 days of missed period in a woman with previous normal cycles. The operation is done as outpatient or office procedure. It is done in aseptic conditions, under sedation if required.

VACUUM ASPIRATION[9]

It is the usual method for first trimester pregnancy termination. Vacuum aspiration may be used for induced abortion as well as therapeutic procedure after spontaneous abortion. It is also used to terminate molar pregnancy.

When used as a spontaneous abortion management or as a therapeutic abortion method, vacuum aspiration may be used alone or with cervical dilatation anytime in the first trimester (up to 12 weeks gestational age). For more advanced pregnancies, vacuum aspiration may be used as one step in a dilatation and evacuation procedure. Vacuum aspiration is the surgical procedure used for almost all first-trimester abortions in many countries, if medication abortion is not a viable option [11].Complications can be reduced by preoperative cervical dilatation.

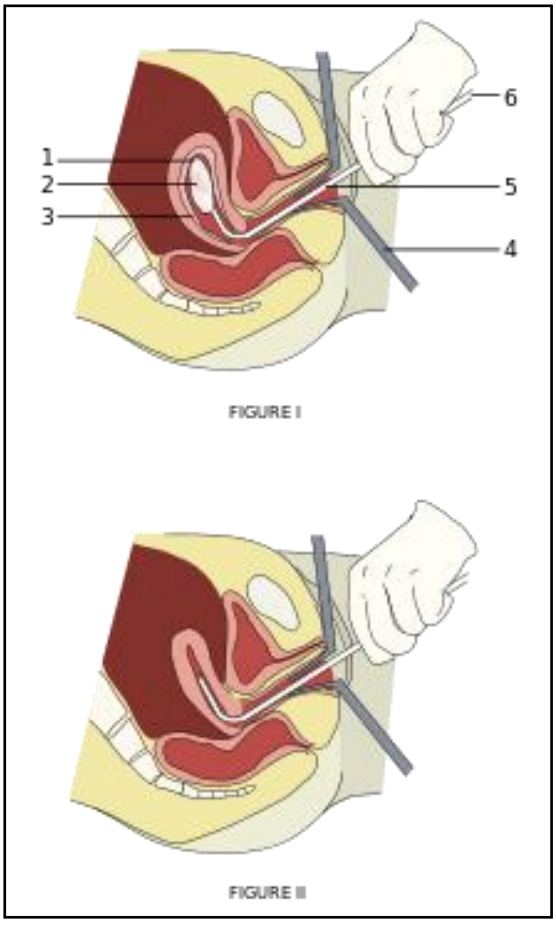


FIGURE I

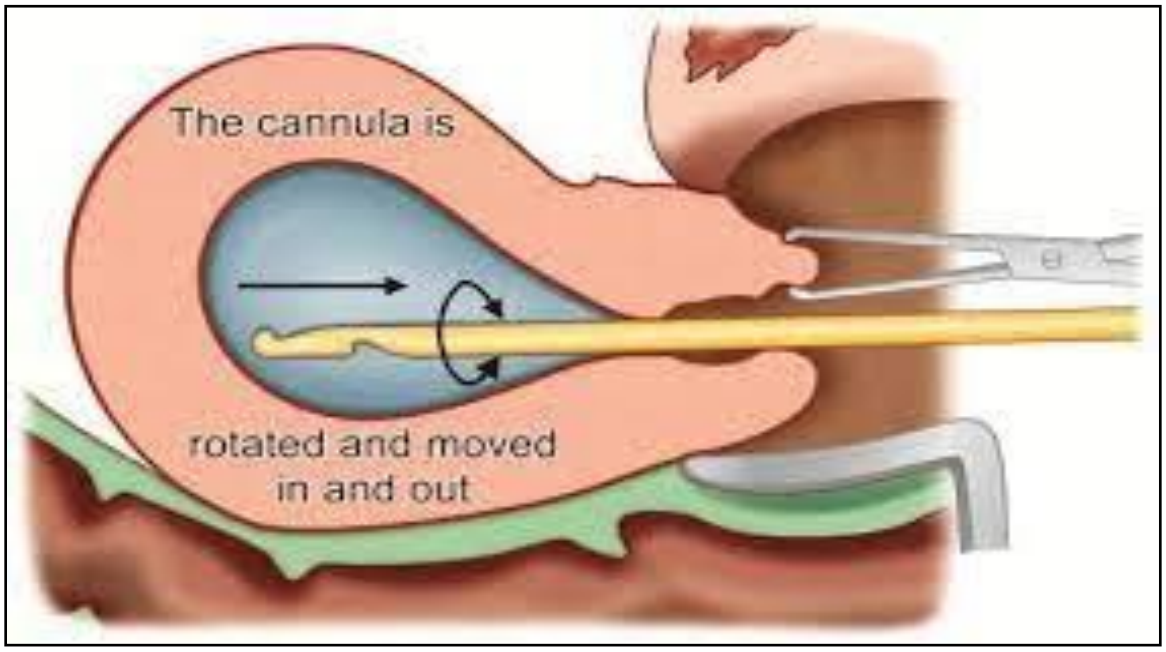
FIGURE II

The World Health Organization's technical and policy guidance on safe abortion and RCOG recommend 'cervical priming before surgical abortion for pregnancy more than 10 weeks' for nulliparous women, age <18 yrs. Cervical dilatation can be achieved through mechanical dilatation, with PG analogues and mifepristone [57].

DILATATION AND EVACUATION

Dilatation and evacuation is the most widely used method for termination of pregnancy up to 16-18 weeks. Cervix is primed by osmotic dilators like Laminaria tents or by pharmacological agents like prostaglandins.

Uterus is evacuated under I/V sedation, short-acting barbiturates, or general anaesthesia. Uterine contents are evacuated by vacuum aspiration using Karman's cannula. Adequate training is an important requirement. With gestational age of 12 weeks, suction evacuation with a wide-bore cannula is sufficient. Oxytocin drip is kept running. D&E is a quicker method as compared with medical methods. But D&E is associated with blood loss and carries a higher risk of traumatic injury to the uterus and cervix [57].



ADVANTAGES OF SURGICAL EVACUATION:

- Very low failure rates (1%)
- Short hospital stay
- Requires less time
- Does not need further follow up to ensure complete evacuation
- Can be combined with IUCD insertion or sterilization operation in the same sitting

DISADVANTAGES OF SURGICAL EVACUATION:

- Requires professional expertise
- Risks of anaesthesia
- Cost of equipment
- May require the patient to remain nil by mouth for an uncertain period of time
- Potential complications of the procedure [12].

IMMEDIATE SURGICAL RISKS:

- Uterine perforation (0.2-1.5%) [55]
- Cervical trauma
- Haemorrhage
- Incomplete evacuation: the second most reported complication, in approximately 2-3% of the procedures [18] [19]
- Infection (incidence ~ 0-10%) [18] [20] [21]. Post-procedural infection is a very common complication encountered.

LATESQUEALAE:

- Endometritis
- Pelvic inflammatory disease
- Salpingitis
- Subsequent infertility
- Increased chances of ectopic pregnancy

The most frequently used surgical procedure for 1st trimester pregnancy termination is suction and evacuation but it is associated with complications like cervical and uterine injuries [2] [3]. Measures to prime or ripen the cervix before suction evacuation (SE) have shown to reduce the risk of cervical injury and of uterine perforation. Pharmacological cervical ripening is preferable to mechanical cervical dilatation as it reduces cervical trauma and increases operative ease. Although many options are available for this purpose [4], misoprostol which is an analogue of the naturally occurring prostaglandins E1 has several advantages over others as it is inexpensive, easily available, does not require refrigeration and has few systemic side-effects. Misoprostol is being administered in

several treatment regimens with varying degree of success for pre abortion cervical ripening [5] [15].

MIFEPRISTONE

In 2002, Drug controller approved the use of Mifepristone (2002) followed by Misoprostol(400mcg) for medical abortion. MTP Act was amended in 2003 to facilitate provision of medical abortion.

Progesterone is an essential hormone in maintaining the pregnancy by having the uterus in inert state. It prevents softening and dilatation of cervix, diminishes prostaglandin output from the decidua, it suppresses uterine contractions by causing hyperpolarisation of cell membrane which makes myocytes less responsive to electrical stimulation [49]. Mifepristone is the only anti-progestin approved for induction of abortion. It is 19-nonsteroid substituted at the 11beta position by a p- di methyl amino phenyl group [50]. It has high resemblance with progesterone receptor, thus inhibits the effect of hormone. Blockage of progesterone receptor leads to vascular damage, decidual necrosis and bleeding. Treatment with mifepristone causes softening of cervix, increases the sensitivity of quiet pregnant uterus into an organ of spontaneous activity. Sensitivity of myometrium increases by five times with maximal effect on cervical ripening and uterine contractility at 36-48hrs following treatment [51].

Mifepristone and prostaglandin analogues act in synergy, hence change in type or dose of one drug or change in the route of administration and interval between mifepristone and PG analogue will have impact on the required dose, subsequent efficacy, and side effects [57].

MISOPROSTOL

Misoprostol was developed in 1973. It is on World Health Organization's List of Essential Medicines. It is a synthetic PGE1 analogue, initially developed for the treatment of peptic ulcer but later used as an abortifacient [53]. It is cheap, stable at room temperature, hence can be stored for a long time. It has minimal effect on bronchi and blood vessels.

It is available as 100microgram and 200 microgram tablets. It contains

- Hydrogenated castor oil
- Hydroxy propyl methylcellulose
- Microcrystalline cellulose

- Sodium starch glucose

It inhibits gastric acid secretion and increases bicarbonate secretion. It is used as a mucoprotective in drug induced gastric ulcer and duodenal ulcer[57].

PHARMACOKINETICS OF MISOPROSTOL

- Misoprostol has rapid absorption after oral administration.
- It is metabolized in the liver and converted to its active metabolite, misoprostol-free acid.
- less than 1% of this metabolite is excreted in urine.
- Plasma concentration peaks at 30mins after oral administration and falls rapidly with a half-life of 20-40mins.
- The level increases gradually and reaches maximum levels after 70-80mins after vaginal administration but remains noticeable for a significantly longer time.

Systemic bioavailability of vaginally administered misoprostol is three times higher than that of orally administered misoprostol. Peak plasma levels occur later with vaginal administration and are lower, but elevated plasma levels are sustained for at least up to 4 hours.

The peak concentration after sublingual administration is like the oral route, but plasma concentration is higher and persistent. Sublingual misoprostol has a higher serum peak concentration and bioavailability compared with the vaginal misoprostol [57].

CLINICAL APPLICATIONS OF MISOPROSTOL

Misoprostol was originally marketed as oral preparation for prevention of peptic ulcers. Early studies performed in late1980's and early 1990's demonstrated that oral administration of misoprostol causes uterine contractions in early pregnancy. Thereafter, misoprostol has been used for various obstetric indications.

- It is used for cervical ripening and labour induction [44] [46]
- Management of uterine atony leading to postpartum haemorrhage
- Management of spontaneous incomplete abortion [47]
- Medical termination of pregnancy in the first trimester (alone or in combination with mifepristone/methotrexate)
- It is used for second trimester (12-20 weeks) termination of pregnancy (in viable fetus) [48]

EFFECT OF MISOPROSTOL ON UTERINE CONTRACTILITY

An ideal agent for induction of abortion is the one which causes uterine contractions subsequent to effective cervical dilatation. PG analogues induce cervical ripening by direct stimulation of myometrium and concomitant effect on the cervix.

The onset of effect of misoprostol and maximum tonus elevation is shorter with oral and sublingual routes compared with vaginal route.

Following single oral administration of misoprostol, regular uterine contractions do not develop. Following sublingual and vaginal administration, uterine contractility is observed after 2 hours of administration.

The uterine contraction is short lasting following sublingual administration than that following vaginal administration. For regimens with mifepristone pre-treatment, less doses of misoprostol are usually required.

MEDICAL ABORTION WITH PROSTAGLANDIN ALONE

Medical abortion with misoprostol alone are effective, though higher doses are needed; side effects are more frequent and induction-abortion interval is longer compared with the combined treatment with mifepristone.

SIDE EFFECS OF MISOPROSTOL

1. Fever

2. Shivering

3. Nausea

4. Vomiting

5. Diarrhoea

6. Abdominal/ uterine cramps

7. Excessive bleeding

CONTRAINDICATIONS OF MISOPROSTOL

1. Ectopic pregnancy

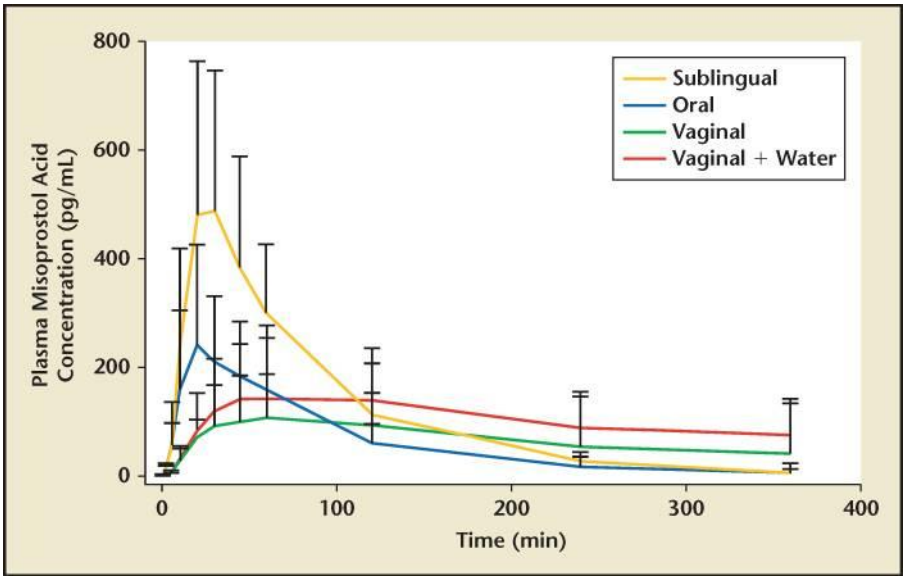
2. Unstable hemodynamic and shock

3. Inflammatory bowel disease

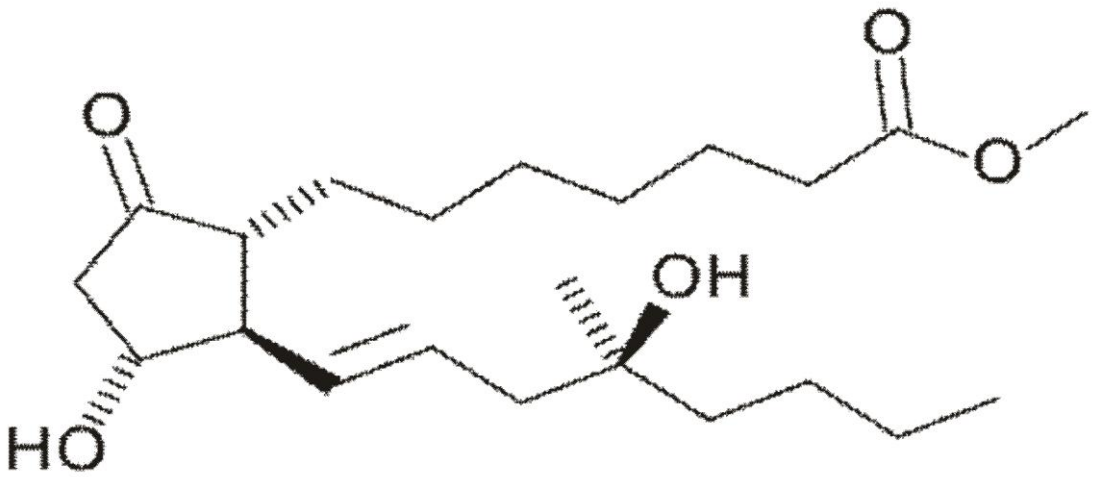
4. Allergy to misoprostol [57]

Many studies have been carried out in different parts of the world to compare the effectiveness of misoprostol as cervical priming agent by different routes before 1st trimester surgical abortion. However, in India studies are very few. The purpose of the current study is to compare the effectiveness and tolerability of misoprostol as a priming agent given by different routes like sublingual, vaginal and oral prior to 1sttrimester surgical abortion [3].

PEAK PLASMA CONCENTRATION OF MISOPROSTOL IN VARIOUS ROUTES



STRUCTURE OF MISOPROST



LITERATURE REVIEW

1. **J. L. Carbonell et al** in 2001 conducted a randomized trial on oral versus vaginal misoprostol for cervical priming in first-trimester abortion. A total of 900 pregnant women, with ages ranging from 18 to 42 years, who asked for pregnancy termination, were included in this study. Women were randomly allocated to one of the following groups: oral administration of 400 mg misoprostol, 8 h before aspiration; and vaginal self-administration of 400 mg misoprostol, 4 h before aspiration. The preoperative cervical dilatation achieved was the main outcome assessed. The cervix was dilated (Hegar) in 348 (78%) subjects from the oral treatment group and in 391 (87%) women from the vaginal treatment group; this difference was statistically significant (p = 0.0004) [3] [8]. The mean dilatation achieved in the oral treatment group was 8.1 mm (SD 1.6 mm) and it was 8.5 mm (SD 1.5 mm) in the vaginal treatment group; this difference was statistically significant (p = 0.0001). The frequencies of side-effects such as nausea, vomiting, diarrhoea and chills reported by women from the vaginal misoprostol group were 10, 8, 18 and 4 times lower, respectively, than those reported by subjects from the oral misoprostol group. In conclusion, vaginal self-administration of misoprostol was the best administration route, as it obtained the same or greater priming effectiveness of the cervix in half the time with a much lower frequency of side-effects [31].
2. **Pikee Saxena et al** in 2004 conducted a study on comparison between the sublingual and oral route of misoprostol for pre-abortion cervical priming in first trimester abortions. A prospective clinical trial was carried out in 100 women with a period of gestation between 6 and 12 weeks who were sequentially allocated to two groups of 50 each. Both groups received 400 mcg of misoprostol 3 h prior to SE by either the sublingual or the oral route. Results showed that for all periods of gestation, sublingual misoprostol significantly improved cervical dilation (P < 0.001) with a reduction in duration of surgery (P = 0.024) compared with the oral route. Mean (6SD) pain scores for the sublingual and oral groups were similar (2.6 6 1.4 versus 3.5 6 1.1). No major complications occurred in either of the two groups. Authors concluded that the sublingual route is an effective alternative to oral administration of misoprostol for cervical dilation. Based on the research so far, this is the first study to compare the efficacy of the sublingual versus the oral route of misoprostol for cervical priming before SE [16] [17] [18].

3. **Leyla Cakir et al** in 2004 conducted a randomized placebo-controlled study on Comparison of oral and vaginal misoprostol for cervical ripening before manual vacuum aspiration of first trimester pregnancy under local anaesthesia. The objective of this prospective randomized placebo-controlled study was to determine the effectiveness of 400 mcg oral and 400 mcg vaginal misoprostol administration for cervical priming 3 h prior to manual vacuum aspiration (MVA) under local anaesthesia for voluntary termination of pregnancy before 10 weeks of gestation in comparison with placebo oral or placebo vaginal administration (n =40 in each group). Post medication cervical dilatation was similar in the oral (mean, 6.6±1.5) and vaginal (mean, 7.2±0.8) misoprostol groups but significantly higher compared with the oral (mean, 3.4±0.2) and vaginal (mean, 3.6±1.9) placebo groups. Duration of the procedure was also significantly shorter in the misoprostol groups in comparison with their placebo counterparts. Preoperative bleeding and side effects were more common in the misoprostol groups, but none required medical intervention. Intraoperative bleeding was less in the vaginal misoprostol group compared with the placebo groups. There was no significant difference in terms of visual analogue scores during the procedure, patient satisfaction, days of postoperative bleeding and rate of postoperative complications among the groups. Cervical priming with misoprostol administered orally or vaginally 3 h before MVA for termination of pregnancy under local anaesthesia facilitates the procedure by decreasing the need for cervical dilatation and by shortening its duration without improving patients pain perception and satisfaction mainly due to side effects [29].
4. **Rebecca H. Allen et al** in 2007 published guidelines on cervical dilation before first-trimester surgical abortion. First-trimester surgical abortion is a common, safe procedure with a major complication rate of less than 1%. Cervical dilation before suction aspiration is usually accomplished using tapered mechanical dilators. Risk factors for major complications in the first trimester are increasing gestational age and provider inexperience. Use of laminaria ten tfor cervical priming reduces the risk of cervical laceration and, to a lesser extent, uterine perforation. While pharmacological priming agents may potentially have the same effects, no published studies to date have been large enough to assess these outcomes. Given an experienced provider, the risk of these injuries during suction aspiration is very small. Cervical priming can be achieved with osmotic dilators or pharmacological agents. The advantages of osmotic

dilators such as laminaria, Dilapan-S™ and Lamicel® are their ability to produce wide cervical dilation, and for the synthetic types, their advantages include predictable effects and rapid onset of action. A disadvantage of osmotic dilators is that they require a speculum examination and a trained clinician to perform the insertion. When cervical priming is performed, misoprostol is the prostaglandin analogue most used worldwide. Compared to laminaria, vaginal misoprostol requires a shorter period to achieve the same dilatation, is associated with less discomfort and is preferred by women. The sublingual route appears as effective as vaginal administration and requires less time for priming (2 h), but it is associated with more side effects. Oral administration can produce equivalent dilation to vaginal or sublingual administration, but higher doses and longer treatment periods (8 to 12 h) are required. Buccal administration of misoprostol appears to have a pharmacokinetic and physiologic profile like vaginal administration; however, there are no published studies of buccal misoprostol prior to first-trimester suction abortion. While extensive data demonstrate that a variety of agents are safe and effective at causing cervical softening and dilation preoperatively, there are not enough data to conclude that routine cervical priming is necessary to reduce complications of first-trimester surgical abortion. Cervical priming increases preoperative cervical dilation, making the procedure easier and quicker for the physician. However, in order to preoperatively dilate the cervix, the woman must receive the agent at least 3 to 4 h prior to her procedure. Besides the additional waiting, the woman might experience bleeding and cramping prior to the procedure. There are insufficient data evaluating how cervical priming affects women's quality of life in relation to abortion. Based on existing evidence, the Society of Family Planning does not recommend routine cervical priming for suction aspiration procedures. The Society of Family Planning further recommends that providers consider cervical priming only for women who may be at increased risk of complications from cervical dilation, including those late in the first trimester, adolescents, and women in whom cervical dilation is expected to be difficult due to either patient factors or provider experience [21].

5. **Pikee Saxena et al** in 2008 conducted a randomised comparison between sublingual, oral and vaginal route of misoprostol for pre-abortion cervical ripening in first-trimester pregnancy termination under local anaesthesia. In a prospective randomised clinical trial, 200 women in the first trimester of pregnancy were randomised into four

groups of 50 each. Patients in control group did not receive any medication before SE while other treatment groups received 400 μg of misoprostol three hours prior to SE either by sublingual/oral or by vaginal route. Main outcome measure was basal cervical dilatation while the secondary outcome measures were operative blood loss, time duration of surgery, patient satisfaction, pain perception and adverse effects. Results showed that sublingual group had a higher dilatation (9.9 ± 2.1 mm; $P < 0.001$) and lesser time duration of surgery (3.6 ± 1.0 min; $P < 0.01$) as compared to oral (8.2 ± 2.6 mm, 4.9 ± 1.7 min) or vaginal routes (7.6 ± 2.6 mm, 5.2 ± 1.8 min). Mean pain score of the sublingual group was significantly lower (2.4 + 1.3; $P < 0.001$) as compared to oral (3.4 ± 1.3) or vaginal routes (3.6 ± 1.2). Patient acceptability was higher for sublingual (53 of 150) and oral routes (62 of 150) as compared to vaginal (35 of 150) route. Authors concluded that sublingual route was significantly more effective than oral or vaginal administration of misoprostol for cervical dilatation. Based on the research so far, this is the first study to simultaneously compare the efficacy of sublingual, oral and vaginal routes of misoprostol for cervical priming before SE [16] [17].

6. **Shagufta Parveen et al** in 2011conducted a study on comparison of sublingual, vaginal, and oral misoprostol in cervical ripening for first trimester abortion. It was a hospital based prospective randomized open labelled parallel study. A total of 150 randomly selected women were divided in three groups for sublingual (S/L), vaginal and oral 400 μg of misoprostol single dose administration. The drug was administered 3-4 hours before SE in the S/L and vaginal groups and 12 h before the procedure in the oral group. Efficacy was assessed based on time taken for ripening, duration of the procedure, intra-operative blood loss, and pain score. The tolerability was noted based on side effects. Results showed that the mean time taken for cervical ripening was less in sublingual administration (3.7±1.2 hr) as compared to the vaginal and oral routes. The S/L group had significant cervical dilatation ($P<0.001$) and the duration of SE was less as compared to the vaginal and oral routes. However, the intraoperative blood loss was more in sublingual as compared to the vaginal and oral groups. The intra-operative pain score of the S/L group was significantly lower (1.9±1.1, $P<0.05$) as compared to the vaginal (2.6±1.7) or oral route (3.3±1.7). Loose motions and nausea/vomiting were more with sublingual and oral routes while blood loss was more

in the vaginal route. Authors concluded that administration of misoprostol by the sublingual route is better than the oral and vaginal routes for cervical ripening [33].

7. **Jayati Nath et al** in 2012 conducted a study to compare the effectiveness and tolerability of misoprostol as a cervical ripening agent in the first trimester abortion through sublingual and vaginal routes of administration. This study was carried out in the department of Obs& Medical College and Research Centre (TMMC&RC). A total of 120 patients were included in the study. They were divided in two groups Group A – 60 patients – sublingual, Group B – 60 patients – vaginal. The drug was administered 3-4 hours before suction and evacuation by sublingual and vaginal routes. Efficacy was assessed based on time taken for ripening, dilatation achieved, duration of the procedure, intraoperative blood loss and pain. The patient‘s tolerability was noted based on side effects. Results showed that the mean time taken for cervical ripening was more in the sublingual group as compared to the vaginal ($P<0.001$).The duration of suction and evacuation was less in sub lingual group as compared to the vaginal route. The mean intraoperative blood loss was more in sublingual as compared to the vaginal group. The intraoperative pain score was comparatively lower in S/L group ($P<0.05$) as compared to the vaginal route. Side effects like loose motions, nausea vomiting was more with sublingual group. Authors concluded that sublingual Misoprostol is an effective and favourable cervical ripening agent for 1st trimester abortions [34].
8. **Awassada Punyashthira et al** in 2014 conducted a randomized controlled trial on the effectiveness of sublingual or oral administration of misoprostol for cervical ripening before manual vacuum aspiration in first trimester termination of pregnancy. A double-blind randomized controlled trial was conducted in first trimester termination of pregnancy cases. Eighty cases were recruited and divided into sublingual and oral groups. Both groups were randomized to receive 400 μg misoprostol two hours prior to MVA. Main outcomes were cervical dilatation, operative time, complications, side effects, pain scores, and patient satisfactions. Results showed that sublingual group had significantly more cervical dilatation and shorter operative time than oral group (7.3 ± 1.5 vs. 5.9 ± 1.4 mm, $p<0.001$ and 5.2 ± 3.3 vs. 7.3 ± 4.6 min, $p = 0.02$, respectively). However, there were similar side effects, pain scores, and patient satisfactions in two groups. The present study had no uterine perforation, cervical tear, haemorrhage, or re-evacuation. Authors concluded that sublingual misoprostol route

was more effective for cervical priming prior to MVA in first trimester therapeutic abortion than oral route [35].

9. **Megha Mathur et al** in 2014 conducted a study on role of sublingual misoprostol for cervical priming in first trimester medical termination of pregnancy. This was a prospective open label study conducted at a tertiary centre. A total 150 patients at 6-12 weeks gestation requesting for MTP were randomized into two groups. Patients in study group (n=75) received sublingual misoprostol three hours before surgical abortion and in control group (n=75) directly underwent surgical abortion without prior cervical priming with misoprostol. The outcomes of both groups were recorded in terms of baseline cervical dilatation, need of additional cervical dilatation, intraoperative blood loss, operative time, and procedure related complications. The results were statistically analysed using student-t test and chi-square test. p-value of <0.05 and <0.001were considered significant and highly significant respectively. Results showed that the mean baseline cervical dilatation was significantly more in study group compared to control group (8.6±1.3mm versus 5±2.3mm; p <0.001) and the operative time and intraoperative blood loss were also less (p<0.001). Higher incidence of side effects like nausea, vomiting and pyrexia were recorded in sublingual misoprostol group but were well tolerable to the patients. Authors concluded that sublingual misoprostol is an effective and safe drug for cervical priming prior to surgical evacuation and has good patient acceptability [36].
10. **Dr Jagadevi S et al** in 2015 conducted a study on comparison of sublingual, vaginal and oral misoprostol in cervical ripening prior to 1st trimester surgical abortion. Hospital based prospective randomized study in which 144 women were divided into 3 groups sublingual, vaginal and oral group and single dose 400µg misoprostol was administered 4 hours prior to evacuation. Efficacy was assessed based on dilation achieved and duration of procedure, the tolerability was evaluated based on the side effects. Results showed that cervical dilatation achieved in sublingual group was better than the other routes and had statistical significance. Duration of procedure was also lesser in sublingual group compared to oral and vaginal group. Side effects were seen in all groups, but vomiting being more common in oral group, nausea, and uterine cramps more common in vaginal group and loose motion was seen only in sublingual groups. Authors concluded that administration of misoprostol by sublingual route is better than the oral and vaginal routes for cervical ripening [37].

11. **K. Preethi** in 2015 conducted a study on assessment of efficacy& safety of 2 different doses of sublingual misoprostol 400µg and 200µg with vaginal misoprostol 400µg in cervical ripening in first trimester abortion. The main objective of the study is to compare the efficacy of two different doses of sublingual misoprostol 200 µg and 400 µg with vaginal misoprostol 400 µg in cervical ripening in women undergoing first trimester abortion. An open label, randomized, prospective study was done in family planning inpatient department in MGMH, Hyderabad. 120 pregnant women with < 12 weeks of gestation requiring suction evacuation for first trimester abortion were enrolled and divided into three groups of 40 each. Groups 1,2,3 received misoprostol 400µg vaginally,400µg sublingually, 200µg sublingually respectively. After 5 hrs of administration the cervical dilatation was measured and suction evacuation was done. Misoprostol 400 µg showed no difference in efficacy when administered by vaginal and sublingual routes. Cervical dilatation was more with sublingual misoprostol 400 µg compared to sublingual misoprostol 200 µg, though there was no significant difference in initiating the process of abortion. Sublingual route is preferred because of easy availability and patient's acceptability. Sublingual misoprostol 200 µg can be preferred to 400 µg as it is associated with less side effects [39].
12. **Sukanya Chamnan et al** in 2016 conducted a randomized controlled trial on comparison of sublingual and vaginal misoprostol for cervical ripening before curettage. The study employed a hospital based prospective randomized controlled trial. A total of 70 patients were randomly divided in two groups for 400 micrograms sublingual and vaginal administration. The drug was administered 6 hours before dilatation and curettage. Efficacy was assessed on cervical dilatation achieved, pain score and vaginal blood loss. The tolerable limit was noted based on side effects. Results showed that the sublingual group had significantly more cervical dilatation than the vaginal group (median cervical dilatation 7 mm vs. 5 mm, $P < 0.001$). Significantly less pain scores (VAS) in sublingual group than vaginal group (3.3 vs. 4.8, $P < 0.001$). Postoperative vaginal blood loss in the sublingual group was significantly greater than the vaginal group (20 ml vs. 10 ml, $P < 0.001$). Other side effects such as fever, chill, nausea, vomiting and diarrhoea did not differ in both groups. Authors concluded that sublingual misoprostol could be more effective for cervical dilatation, but presents greater postoperative vaginal blood loss than vaginal route [40].

13. **Taher Mohamed Mostafa El-Barbary** in 2016 conducted a study on misoprostol in missed abortion: oral or vaginal. One hundred and twenty women with first trimester missed abortions were divided into 2 study groups, randomized for oral and vaginal (800 μg) misoprostol, and 2 control groups randomized for oral and vaginal placebo, before undergoing surgical evacuation of conception after 3 hours. Measured outcomes were: post medication cervical dilatation, time needed to dilate the cervix surgically, blood loss, and development of the side effects of misoprostol. The results were post medication cervical dilatation was 7.77 ± 1.22 mm for the vaginal misoprostol group, 7.07 ± 1.36 mm for oral misoprostol, versus 2.43 ± 0.5 mm for the control groups. Post medication cervical dilatation was significantly higher in the vaginal misoprostol group, compared to the oral group (p=0.032†). There were no significant differences in the amount of blood loss between oral (p=0.74), and vaginal misoprostol groups (p=0.629), and gastrointestinal side effects were significantly more in the oral misoprostol group (p=0.014). We concluded that misoprostol is an effective cervical priming agent when administered either orally or vaginally before evacuation of conception in the termination of the first trimester missed abortions [41].
14. **Fariba Farhadifar et al** in 2016 conducted a study on comparison of oral versus vaginal misoprostol for legal abortion in Iranian women. This randomized double-blind clinical trial study was performed on 70 pregnant women applying for abortion. Pregnant women were divided randomly into two groups - oral misoprostol and vaginal misoprostol. In both groups, misoprostol 200 μg every 6 hours up to six times (36 hours) was used. To make the study double-blind, placebo was used. The effectiveness of misoprostol (the expulsion of gestation products) and its side effects (bleeding, fever, etc.) were studied in two groups. The results showed that there were no significant differences statistically between oral (82.3%) and vaginal (80%) misoprostol groups in terms of response to treatment (the expulsion of gestation products). Intervals of consuming oral misoprostol pills to the expulsion of gestation products in the oral and vaginal groups were 4.09 ± 1.56 and 3.67 ± 1.4 hours, respectively (P > 0.05). In terms of complications, only two cases of oral misoprostol group experienced complications. Authors concluded that although the risk of complications in oral method and the need for curettage in vaginal group is high, effectiveness of oral and vaginal misoprostol for induction of legal abortion is similar [42].

15. **Divya Sinha et al** in 2017 conduct a study of oral, sub-lingual and vaginal route of misoprostol as cervical ripening agent before surgical method of termination of first-trimester pregnancy. It was a prospective hospital based randomised study. Total 150 patients at 6-12 weeks gestation requesting for medical termination of pregnancy were divided equally into 3 groups. Every group was advised to have single dose of 400 mcg misoprostol either by oral, sublingual, or vaginal route respectively 4 hours before suction and evacuation. Results showed that the sublingual group had highly significant cervical dilatation (P<0.001) and the duration of suction and evacuation was less as compared to the vaginal and oral routes (p<0.000). However, the mean intraoperative blood loss was more in sublingual as compared to the vaginal and oral groups. Loose motions and nausea/vomiting were more with oral routes. Authors concluded that sublingual route of misoprostol is preferable than oral or vaginal route as pre-abortion cervical ripening agent [43].
16. **Uzma Butt et al** in 2017 conducted a study on comparison of cervical ripening in oral versus vaginal misoprostol administration before surgical termination of first trimester pregnancy. After approval from ethical committee, 150 patients, who fulfilled the inclusion and exclusion criteria, were recruited for the study, and divided into two equal groups, A and B. Patients in group A were given 400µg vaginal misoprostol placed in the posterior fornix of the vagina and patients in group B were given 400µg oral misoprostol. The post-medication cervical ripening was measured. All patients underwent suction evacuation 3 hours after administration of tablet and were observed for 2 hours postoperatively for any allergy or side effects. Results showed that the mean age in group-A (400µg misoprostol vaginally) and in group-B (400µg oral misoprostol) was 26.67±3.93 years and 26.08±5.15 years respectively with similar age distribution. The mean gestational age was 10.93±1.61 weeks in group-A and 10.60±1.62 weeks with no significant difference, p-value > 0.05. The mean cervical dilatation was significantly higher in group-A (6.29±0.85 mm) when compared to group-B (5±0.82 mm), p-value < 0.001. Authors concluded that misoprostol is effective for cervical ripening when administered vaginally before suction evacuation [44].
17. **Varsha Kotwal** in 2020 conducted a study on potency and acceptability of oral misoprostol compared with vaginal misoprostol prior to first trimester abortion. One hundred twenty patients who voluntarily opted for termination of pregnancy were

randomly divided into oral misoprostol group and vaginal misoprostol group. The patients were given 400μgm of misoprostol either by oral route or by vaginal administration 4 hours before surgical termination of pregnancy. The data collection was done which was based on questionnaire system, vaginal bleeding and abdominal pain was noted. Results showed that there was no significant difference in oral and vaginal misoprostol as far as cervical dilatation is concerned (5.63mm versus 5.43mm). The women in vaginal group experienced more bleeding 42% versus 24% in oral group. A total of 89% patients in oral misoprostol group expressed their satisfaction whereas a total number of 75% patients in vaginal misoprostol group were satisfied. Authors concluded that the effectiveness of oral misoprostol is similar to vaginal misoprostol for cervical ripening but women are more satisfied in oral misoprostol group than vaginal group [45].

18. **Behnaz Souizi et al** in 2020 conducted an open label randomized clinical trial study on 172 individuals on Comparison of the efficacy of sublingual, oral, and vaginal administration of misoprostol in the medical treatment of missed abortion during first trimester of pregnancy. The participants were randomized using permuted blocks of six. A dose of 600 μg of misoprostol every 6 h (maximum of 4 doses) was administrated to each group. Higham chart and demographic questionnaires were completed by the investigator. Data were analysed using Stata software version 12. Results showed that the mean age of the participants was 29.81 ± 6.7 years, and the mean gestational age was 8.45 ± 2.32 weeks. We found a significant difference regarding the abortion success rate and the time interval between the administration of the drug among three groups (P = 0.036 and < 0.001 in turn). There was no statistically significant difference between the three groups in terms of severity and duration of vaginal bleeding until day 7 after induction (P = 0.091 and 0.143, respectively). Furthermore, we found statistically significant differences in some drugs, which induced side effects namely vomiting and headache, between the three groups (P = 0.032 and 0.028 in turn). Authors concluded that the findings suggest that vaginal administration of misoprostol is more successful than the sublingual and oral route for complete abortion; vaginal administration of misoprostol is an appropriate alternative to curettage [46].
19. **Dr Harpreet Kaur et al** in 2020 showedastudy of sub-lingual, vaginal, and oral misoprostol in cervical ripening for first trimester abortions. It was a prospective

longitudinal study conducted in Department of Obstetrics and Gynaecology, Guru Gobind Singh Medical College, Faridkot, Punjab from Jan 2019 to Dec 2019 on 60 women seeking first trimester abortions who were given misoprostol 400 μg by sublingual, vaginal and oral routes for cervical ripening prior to surgical evacuation. It was found that cervical dilatation was better in sublingual group as compared to oral or vaginal group and the mean duration of surgery was also less in sublingual group than in vaginal or oral group. So, it was concluded that sublingual misoprostol is more effective than vaginal or oral route for pre-operative cervical ripening in first trimester abortion [47].

MATERIAL AND METHODS

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This prospective randomised non blind study entitled 'Comparison of sublingual, oral and vaginal misoprostol for cervical ripening before first trimester abortion' was conducted after clearance from Institutional Ethical Committee, in the department of Obstetrics and Gynaecology, Santosh Medical College and Hospital, Ghaziabad, UP during the period of June2021-August 2022.

1) Study Population:

   Patients with a history of amenorrhea and period of gestation up to 12 weeks who gave consent for surgical abortion were enrolled and given tablet misoprostol 400mcg, 4 hours prior to the surgical abortion by one of the following routes:

   - Sub-lingual
   - Oral
   - Vaginal

2) Study Design:

   Prospective randomized non blind study.

3) Study Place:

   Department of Obstetrics and Gynaecology,

   Santosh medical college and hospital, Ghaziabad, UP

4) Period of Study:

   One year

5) Sample Size:

$$n = \frac{2\left(Z_{\alpha}{}^{2} + Z_{\beta}{}^{2}\right)\sigma^{2}}{(\mu_1 - \mu_2)^2}$$

By using the above formula my sample size was calculated to be 120(40 in each group)

6) Inclusion criteria:

   - Singleton pregnancy
   - intrauterine pregnancy
   - Period of gestation <12 weeks.
   - Patients willing to give informed consent.
   - Closed cervical OS on digital examination.

7) Exclusion criteria:

- Multiple pregnancy
- Patients with complaint of vaginal bleeding.
- Patients with inevitable/threatened abortion
- History of hypersensitivity to prostaglandins
- Haemoglobin (HB) level <9 g/dl
- History of any heart disease/renal disease/coagulopathy/active infection

STUDY PROCEDURE

After approval from institutional ethical committee, patients were randomly recruited from Obstetrics OPD of Department of Obstetrics and Gynaecology of Santosh Medical College & Hospital, Ghaziabad as per inclusion and exclusion criteria.

A **detailed history** was taken and an examination including per speculum and per vaginal examination was done. Routine & appropriate investigations were done for all the patients. Period of gestation was calculated from the last menstrual period (LMP). The patients and the attendants were explained about the procedure and Informed consent was taken from all patients.

Physical Examination

- A thorough general examination (including pulse & blood pressure) was done to check for any general disease. Systemic examination was performed to rule out cardiovascular and respiratory problems [6].
- Bimanual examination was done for a rough estimate of the gestational age [6].

Investigations

1) Routine investigations

- Haemoglobin
- Blood grouping & Rhesus typing
- Urine routine examination
- Random blood sugar
- Bleeding time, Clotting time, Platelet count
- HIV & HBs Ag, HCV

2) An Ultrasonography (USG) examination to confirm period of gestation and to rule out ectopic pregnancy and multiple pregnancy

Patients were randomly divided into three groups of 40 patients each

- **Group A (Sub-Lingual Misoprostol)**
- **Group B (Oral Misoprostol)**
- **Group C (Vaginal Misoprostol)**

After randomization by envelope method, 400mcg of misoprostol was given either sub-lingually, orally, or vaginally 4 hours prior to the suction evacuation. Pre-operative side effects like vomiting, diarrhoea, abdominal cramps, bleeding per vaginum and fever were enquired about and noted. Suction evacuation was done under IV Sedation or short GA. Efficacy in all the three groups was assessed by cervical dilatation which was measured by the maximum size of Hegar's dilator passing through the cervical os without resistance. Other primary outcome parameter assessed was intra-operative blood loss – the total amount of blood in suction tube and container was measured after sieving the product of conception. Appropriate amount of liquor for corresponding period of gestation was subtracted to get the amount of actual blood loss. Operative time was measured from the start of cervical dilatation till the end of evacuation i.e end of uterine curettage. Any intra-operative complications were noted. Post-operatively all patients were given analgesics and antibiotics and advised for follow-up after 7 days and after the first menstrual period. They were advised to report earlier in case of severe bleeding, fever, or abdominal pain. During the follow-up visit, any side effects or complications were enquired about and noted.

STATISTICAL ANALYSIS

STATISTICAL ANALYSIS

The presentation of the Categorical variables was done in the form of number and percentage (%). On the other hand, the presentation of the continuous variables was done as mean ± SD and median values. The following statistical tests were applied for the results:

1. The comparison of the variables which were quantitative in nature were analyzed using ANOVA (for normally distributed data) and a Post Hoc test (Bonferroni correction) was applied.

2. The comparison of the variables which were qualitative in nature were analyzed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

The data entry was done in the Microsoft Excel spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 25.0.For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS

AND

OBSERVATION

RESULTS AND OBSERVATION

This prospective randomised non blind study entitled 'Comparison of sublingual, oral and vaginal misoprostol for cervical ripening before first trimester abortion' was conducted after clearance from Institutional Ethical Committee, in the department of Obstetrics and Gynaecology, Santosh Medical College and Hospital, Ghaziabad, UP, during the period of June2021-August 2022. The sample size obtained was 120 and the patients were randomly allocated into 3 study groups.

Table 1: -Comparison of Age(years) between group A, B and C.

Age(years)	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
18-20	4 (10%)	2 (5%)	5 (12.50%)	0.532* A vs B:0.74* A vs C:0.415* B vs C:0.351*
21-30	29 (72.50%)	32 (80%)	32 (80%)	
31-40	7 (17.50%)	6 (15%)	3 (7.50%)	
Mean ± SD	25.98 ± 4.94	25.58 ± 4.09	25.35 ± 3.77	0.805‡ A vs B:0.678 A vs C:0.517 B vs C:0.815
Median(25th-75th percentile)	25.5 (22-28)	25 (22-29)	25.5 (22-28.25)	
Range	19-37	18-34	19-32	

* Fisher's exact test, ‡ ANOVA

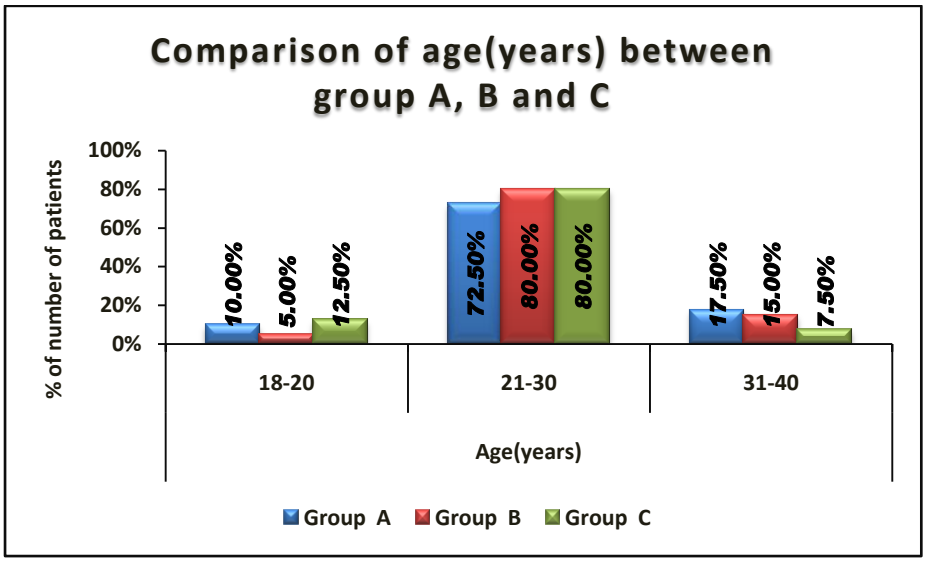

Figure 1: -Comparison of Age(years) between group A, B and C

Distribution of age was comparable between group A, B and C. (18-20 years: - 10% vs 5% vs 12.50% respectively, 21-30 years: - 72.50% vs 80% vs 80% respectively, 31-40 years: - 17.50% vs 15% vs 7.50% respectively) (p value=0.532) as shown in table 1, figure 1. Mean ± SD of age(years) in group A was 25.98 ± 4.94, group B was 25.58 ± 4.09 and group C was 25.35 ± 3.77 with no significant difference between them. (p value=0.805))

Table 2: -Comparison of Religion between group A, B and C.

Religion	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
Hindu	17 (42.50%)	15 (37.50%)	17 (42.50%)	0.78* A vsB:0.732* A vsC:0.622* B vsC:0.82*
Islam	21 (52.50%)	24 (60%)	23 (57.50%)	
Others	2 (5%)	1 (2.50%)	0 (0%)	
Total	40 (100%)	40 (100%)	40 (100%)	

* **Fisher's exact test**

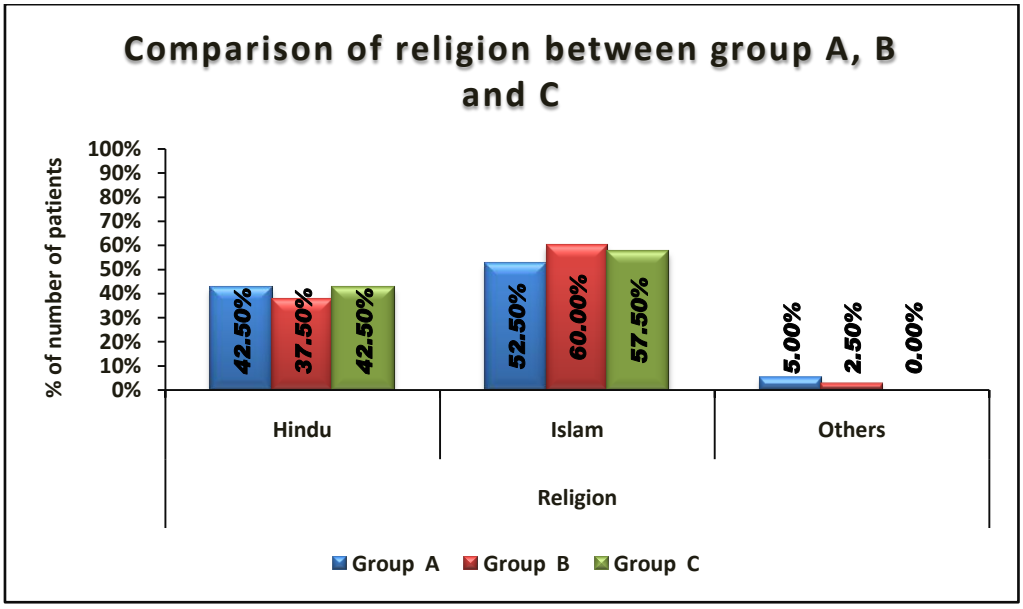

Figure 2: -Comparison of religion between group A, B and C.

Distribution of religion was comparable between group A, B and C. (Hindu: - 42.50% vs 37.50% vs 42.50% respectively, Islam: - 52.50% vs 60% vs 57.50% respectively, Others: - 5% vs 2.50% vs 0% respectively) (p value=0.78) as shown in table 2, figure 2.

Table 3: -Comparison of locality between group A, B and C.

Locality	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
Rural	6 (15%)	9 (22.50%)	8 (20%)	0.686†
Urban	34 (85%)	31 (77.50%)	32 (80%)	A vs B:0.39† A vs C:0.556† B vs C:0.785†
Total	40 (100%)	40 (100%)	40 (100%)	

† **Chi square test**

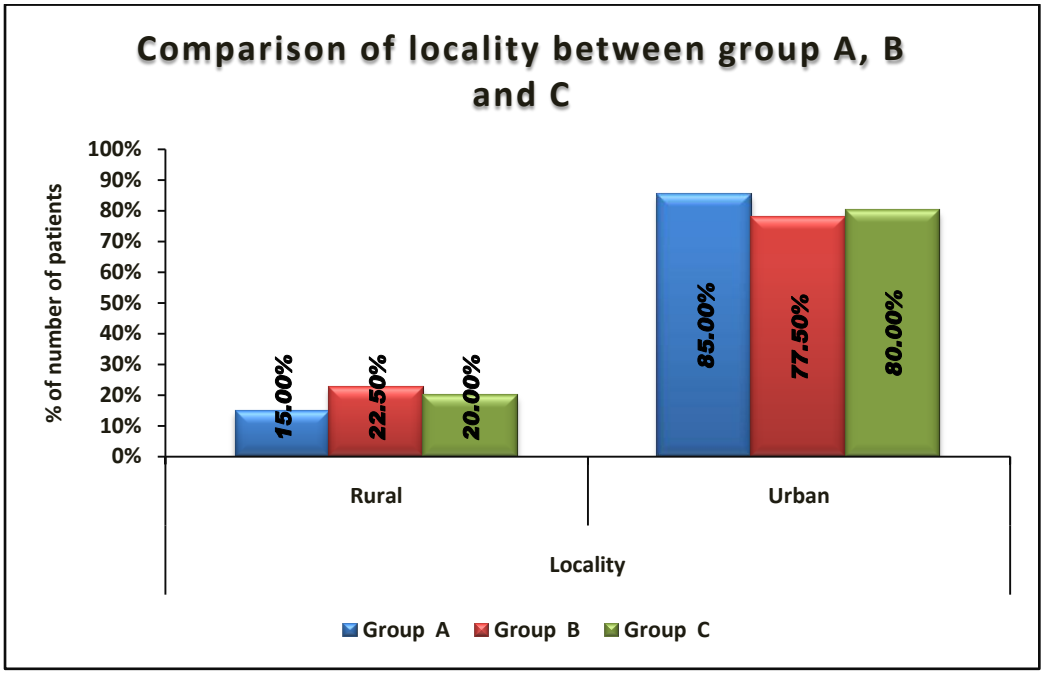

Figure 3: -Comparison of locality between group A, B and C.

Distribution of locality was comparable between group A, B and C. (Rural: - 15% vs 22.50% vs 20% respectively, Urban: - 85% vs 77.50% vs 80% respectively) (p value=0.686).

It is shown in table 3, figure 3.

Table 4: -Comparison of Education between group A, B and C.

Education	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
Illiterate	8 (20%)	9 (22.50%)	7 (17.50%)	
Primary school	19 (47.50%)	18 (45%)	21 (52.50%)	0.99*
Secondary school	9 (22.50%)	10 (25%)	8 (20%)	A vs B:1*
Graduate	4 (10%)	3 (7.50%)	4 (10%)	A vs C:0.972*
Total	40 (100%)	40 (100%)	40 (100%)	B vs C:0.831*

* **Fisher's exact test**

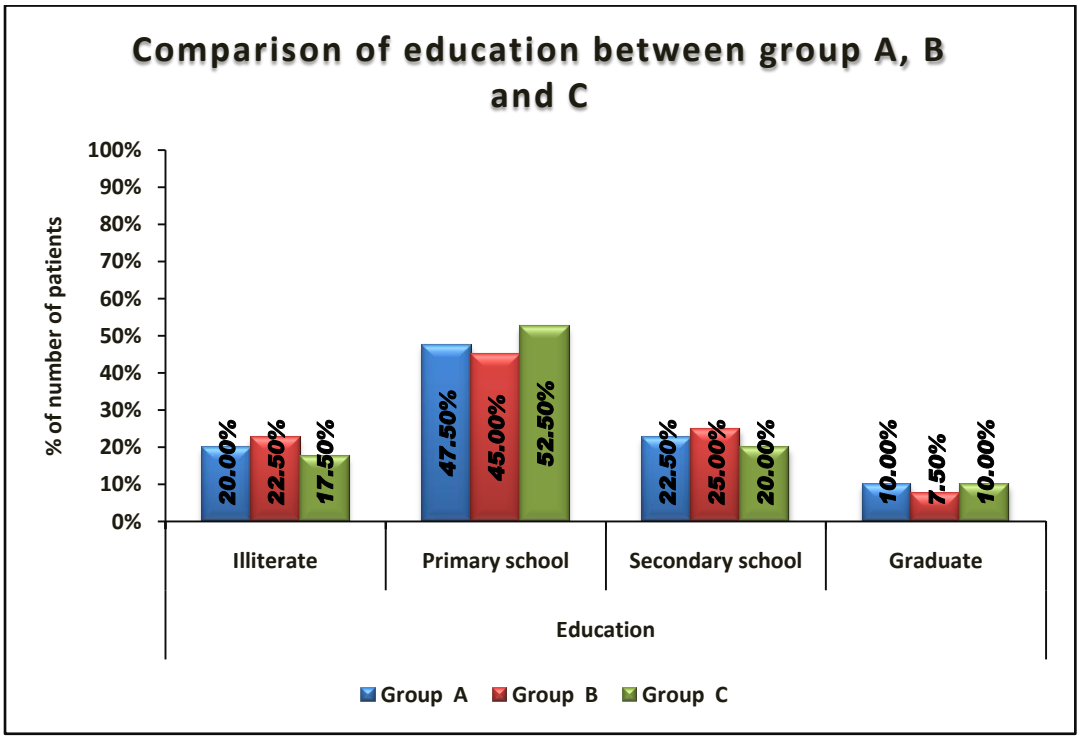

Figure 4: -Comparison of Education between group A, B and C.

Distribution of education was comparable between group A, B and C. (Illiterate: - 20% vs 22.50% vs 17.50% respectively, Primary school: - 47.50% vs 45% vs 52.50% respectively, Secondary school: - 22.50% vs 25% vs 20% respectively, Graduate: - 10% vs 7.50% vs 10% respectively) (p value=0.99) as shown in table 4, figure 4.

Table 5: -Comparison of Gravida Status between group A, B and C.

Gravida	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
Primigravida	14 (35%)	14 (35%)	9 (22.50%)	
G2	15 (37.50%)	13 (32.50%)	11 (27.50%)	0.275†
G3	8 (20%)	8 (20%)	9 (22.50%)	A vs B:0.918*
>G3	3 (7.50%)	5 (12.50%)	11 (27.50%)	A vs C:0.097†
Total	40 (100%)	40 (100%)	40 (100%)	B vs C:0.313†

* Fisher's exact test, † Chi square test

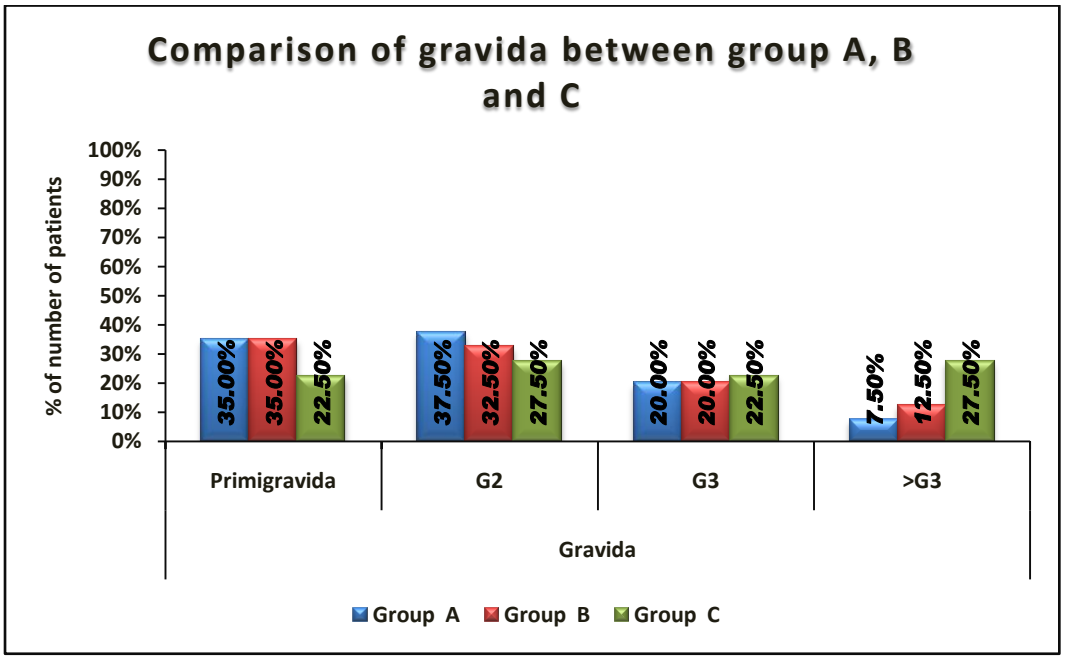

Figure 5: -Comparison of GravidaStatusbetween group A, B and C.

Gravida status was comparable between group A, B and C. (Primigravida: - 35% vs 35% vs 22.50% respectively, G2: - 37.50% vs 32.50% vs 27.50% respectively, G3: - 20% vs 20% vs 22.50% respectively, >G3: - 7.50% vs 12.50% vs 27.50% respectively) (p value=0.275) as shown in table 5, figure 5.

Table 6: -Comparison of Period of Gestation(weeks) between group A, B and C.

Period of Gestation(weeks)	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
Mean ± SD	10.71 ± 2.25	12.24 ± 2.05	10.73 ± 1.38	0.0004‡
Median (25th-75th percentile)	10.79 (9-12.571)	12 (10.679-14)	11 (9.679-11.679)	A vs B:0.0006 A vs C:0.96
Range	6.43-14.71	7.71-16.14	8.29-14	B vs C:0.0007

‡ ANOVA

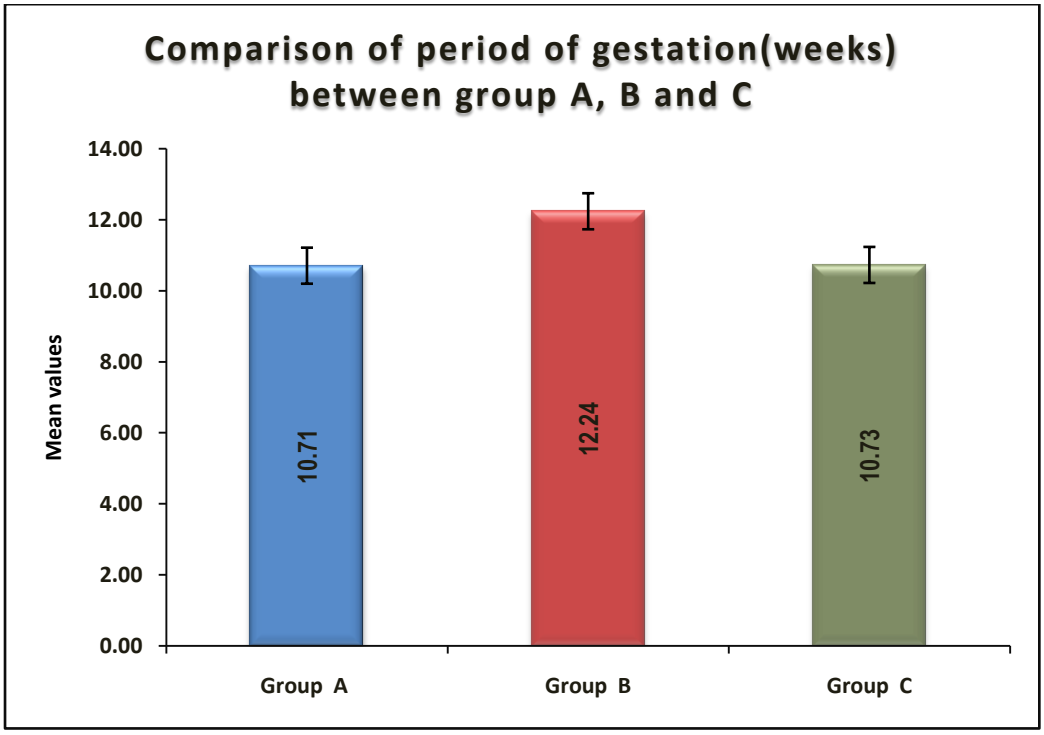

Figure 6: -Comparison of period of gestation(weeks) between group A, B and C.

As shown in table 6, figure 6, Mean ± SD of period of gestation(weeks) in group B was 12.24 ± 2.05 which was significantly higher as compared to group C (10.73 ± 1.38, p value=0.0007) and group A (10.71 ± 2.25, p value=0.0006). Period of gestation(weeks) was comparable between group A and C. (p value=0.96)

Table 7 :- Convenience/Acceptance of Route of Administration

Convenience /Acceptance	Vaginal	Sub lingual	Oral
YES	9	29	32
NO	31	11	8
Percentage	22.5%	72.5%	80%

In our study, 77.5% of patients in the vaginal group did not find vaginal route convenient & acceptable, only 22.5% of patients accepted vaginal route willingly. Whereas 80% of patients in oral group and 72.5% of patients in sublingual group found the respective route of administration convenient.

Table 8:-Comparison of patient characteristics between group A, B and C.

Patient characteristics	Group A(n=40)	Group B(n=40)	Group C(n=40)
Age(years)	25.98 ± 4.94	25.58 ± 4.09	25.35 ± 3.77
Period of gestation(Weeks)	10.71 ± 2.25	12.24 ± 2.05	10.73 ± 1.38
Gravida	2.02 ± 1	2.15 ± 1.17	2.68 ± 1.35
Parity	0.68 ± 0.73	0.85 ± 0.8	1.27 ± 0.93
RELIGION			
Hindu	17 (42.50%)	15 (37.50%)	17 (42.50%)
Islam	21 (52.50%)	24 (60%)	23 (57.50%)
Others	2 (5%)	1 (2.50%)	0 (0%)
RESIDENCE			
Rural	6 (15%)	9 (22.50%)	8 (20%)
Urban	34 (85%)	31 (77.50%)	32 (80%)
EDUCATION			
Illiterate	8 (20%)	9 (22.50%)	7 (17.50%)
Primary school	19 (47.50%)	18 (45%)	21 (52.50%)
Secondary school	9 (22.50%)	10 (25%)	8 (20%)
Graduate	4 (10%)	3 (7.50%)	4 (10%)
Previous abortion	12 (30%)	10(25%)	11 (27.5%)

*** Fisher's exact test, † Chi square test, ‡ ANOVA**

PRIMARY OUTCOME OF THE STUDY

Table 9: -Comparison of cervical dilatation between group A, B and C.

Cervical dilatation	Group A (n=40)	Group B (n=40)	Group C (n=40)	P value
5mm	0 (0%)	12 (30%)	5 (12.50%)	<.0001† A vs B:<.0001† A vs C:<.0001* B vs C:0.056†
5 to 8 mm	0 (0%)	28 (70%)	35 (87.50%)	
8 to 10 mm	40 (100%)	0 (0%)	0 (0%)	
Total	40 (100%)	40 (100%)	40 (100%)	

* Fisher's exact test, † Chi square test

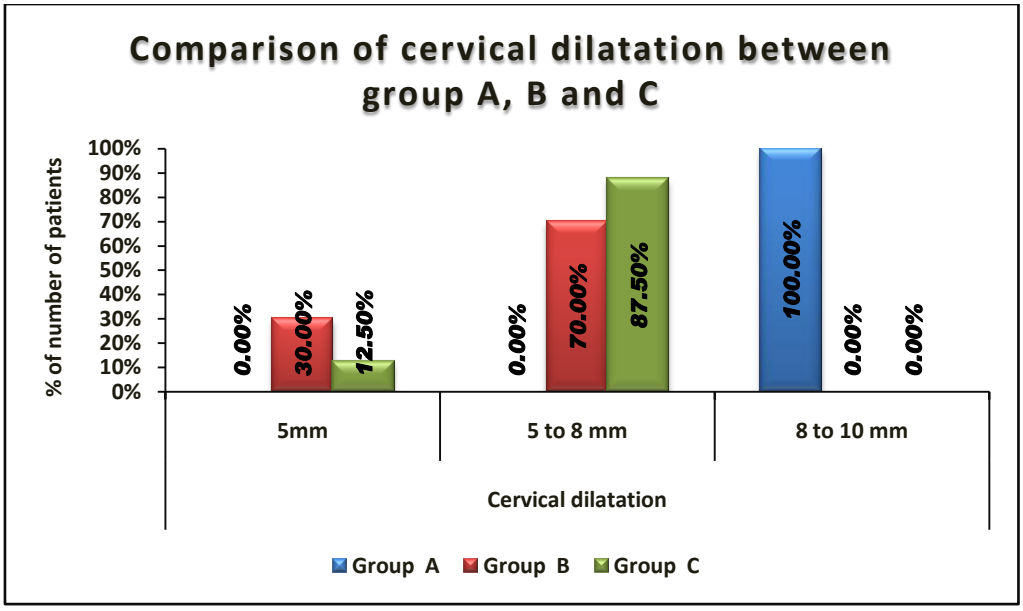

Figure 9: -Comparison of cervical dilatation between group A, B and C.

Proportion of patients with cervical dilatation of 8 to 10 mm was significantly higher in group A as compared to group B (p value<.0001) and group C (p value<.0001). (8 to 10 mm: - 100% vs 0%, 0% respectively). Proportion of patients with cervical dilatation of 5mm and 5 to 8 mm was significantly higher in group B and C as compared to group A. (5mm:- 30%, 12.50% vs 0% respectively, 5 to 8 mm:- 70%, 87.50% vs 0% respectively).

Distribution of cervical dilatation was comparable between group B and C. (p value=0.056) as shown in table 9, figure 9.

Table 10: -Comparison of duration of procedure (minutes) between group A, B and C.

Duration of procedure (minutes)	Group A (n=40)	Group B (n=40)	Group C(n=40)	P value
Mean ± SD	8.12 ± 3.14	10.25 ± 4.32	9.88 ± 3.84	<.0003‡
Median(25th-75th percentile)	10 (8-10)	12 (10-12)	10 (8-10)	A vs B:<.0001 A vs C:0.041
Range	5-12	5-12	5-12	B vs C:0.0001

‡ ANOVA

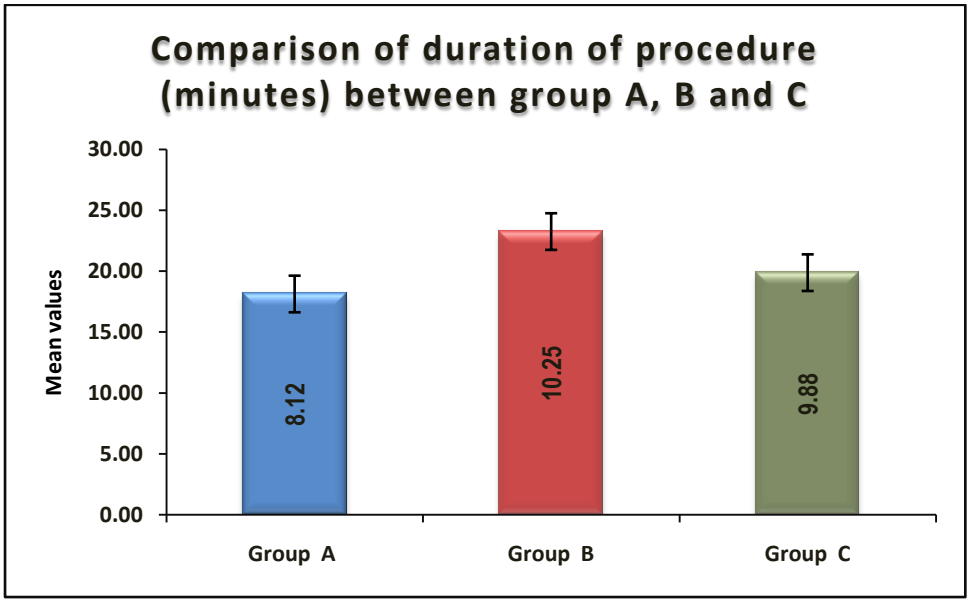

Figure 10: -Comparison of duration of procedure (minutes) between group A, B and C.

Mean ± SD of duration of procedure (minutes) in group B was 10.25 ± 4.32 which was significantly higher as compared to group C (9.88 ± 3.84, p value=0.0001) and group A (8.12 ± 3.14, p value<.0003).

Mean ± SD of duration of procedure (minutes) in group C was significantly higher as compared to group A. (p value=0.041) as shown in table 10, figure 10. Hence the operative time was highest in oral group and least in sub-lingual group.

Table 11: -Comparison of Intra Operative Blood Loss between Group A, B and C.

Intra operative blood loss	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
Mild/moderate	39 (97.50%)	37 (92.50%)	14 (35%)	<.0001† A vs B:0.615* A vs C:<.0001* B vs C:<.0001*
Severe	1 (2.50%)	3 (7.50%)	26 (65%)	
Total	40 (100%)	40 (100%)	40 (100%)	

* Fisher's exact test, † Chi square test

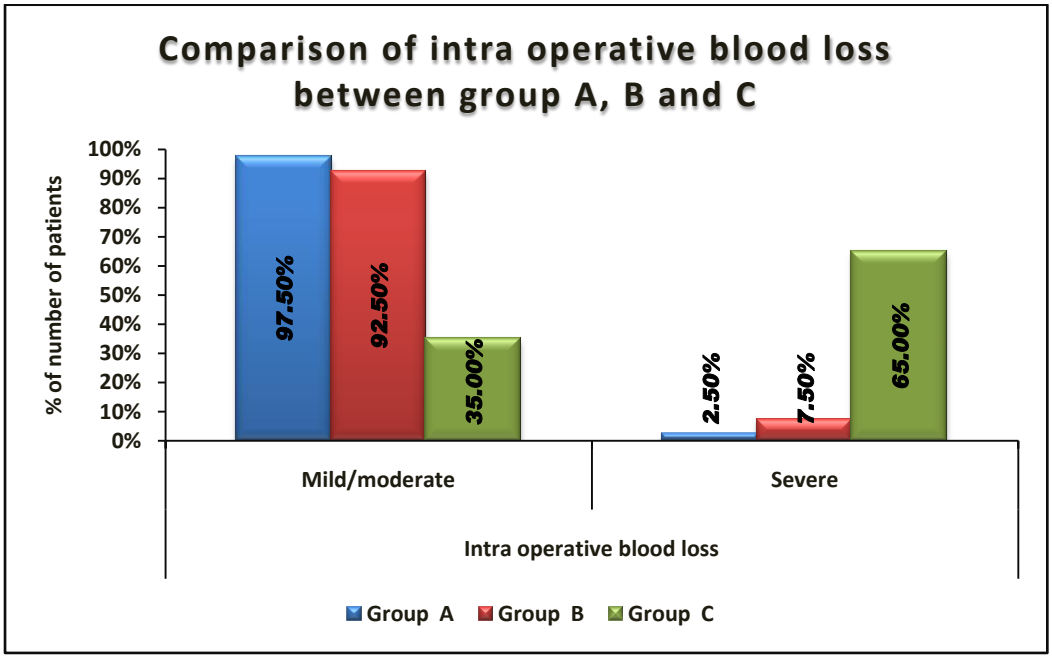

Figure 11: -Comparison of intra operative blood loss between group A, B and C.

Proportion of patients with mild/moderate intra operative blood losswas significantly higher in group A and group B as compared to group C. (p value<.0001) (Mild/moderate blood loss: - 97.50%, 92.50% vs 35% respectively). Proportion of patients with intra operative blood loss of severe degree was significantly higher in group C as compared to group A (p value <.0001) and group B (p value<.0001). (Severe: - 65% vs 2.50%, 7.50% respectively).

Distribution of intra operative blood loss was comparable between group A and B. (p value=0.615) It is shown in table 11, figure 11.

Table 12:-Comparison of intra-operative characteristics between group A, B and C.

Intra-operative characteristics	Group A(n=40)	Group B(n=40)	Group C(n=40)
CERVICAL DILATAION			
5mm	0 (0%)	12 (30%)	5 (12.50%)
5 to 8 mm	0 (0%)	28 (70%)	35 (87.50%)
8 to 10 mm	40 (100%)	0 (0%)	0 (0%)
INTRA OPERATIVE BLOOD LOSS			
Mild/moderate	39 (97.50%)	37 (92.50%)	14 (35%)
Severe	1 (2.50%)	3 (7.50%)	26 (65%)
PAIN SCORE			
Mild	17 (42.50%)	18 (45%)	16 (40%)
Moderate	16 (40%)	9 (22.50%)	21 (52.50%)
Severe	7 (17.50%)	13 (32.50%)	3 (7.50%)
DURATION OF PROCEDURE (in minutes)	8.12 ± 3.14	10.25 ± 4.32	9.88 ± 3.84

† Chi square test, ‡ ANOVA

ADVERSE EFFECTS

Table 13: -Comparison of Vomiting between group A, B and C.

Vomiting	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
No	37 (92.50%)	37 (92.50%)	40 (100%)	0.244*
Yes	3 (7.50%)	3 (7.50%)	0 (0%)	A vs B:1*
Total	40 (100%)	40 (100%)	40 (100%)	A vs C:0.241*
				B vs C:0.241*

* Fisher's exact test

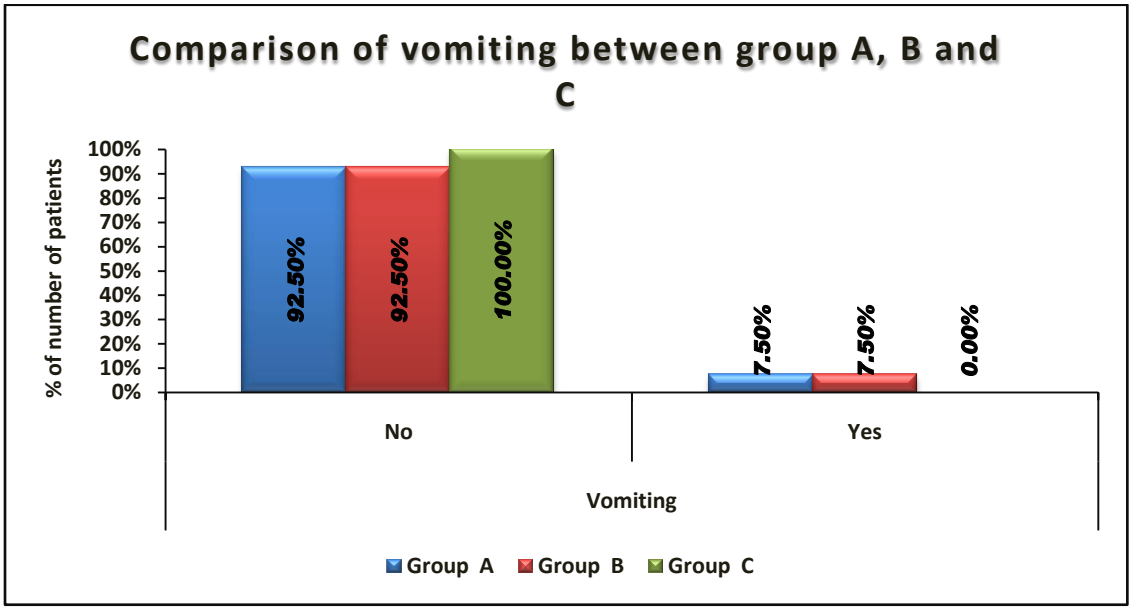

Figure 13: -Comparison of vomiting between group A, B and C.

Distribution of vomiting was comparable between group A, B and C. (7.50% vs 7.50% vs 0% respectively) (p value=0.244) as shown in table 13, figure 13.

Table 14: -Comparison of Loose Motion between group A, B and C.

Loose motion	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
No	39 (97.50%)	33 (82.50%)	40 (100%)	0.006* A vs B:0.057* A vs C:1* B vs C:0.012*
Yes	1 (2.50%)	7 (17.50%)	0 (0%)	
Total	40 (100%)	40 (100%)	40 (100%)	

* Fisher's exact test

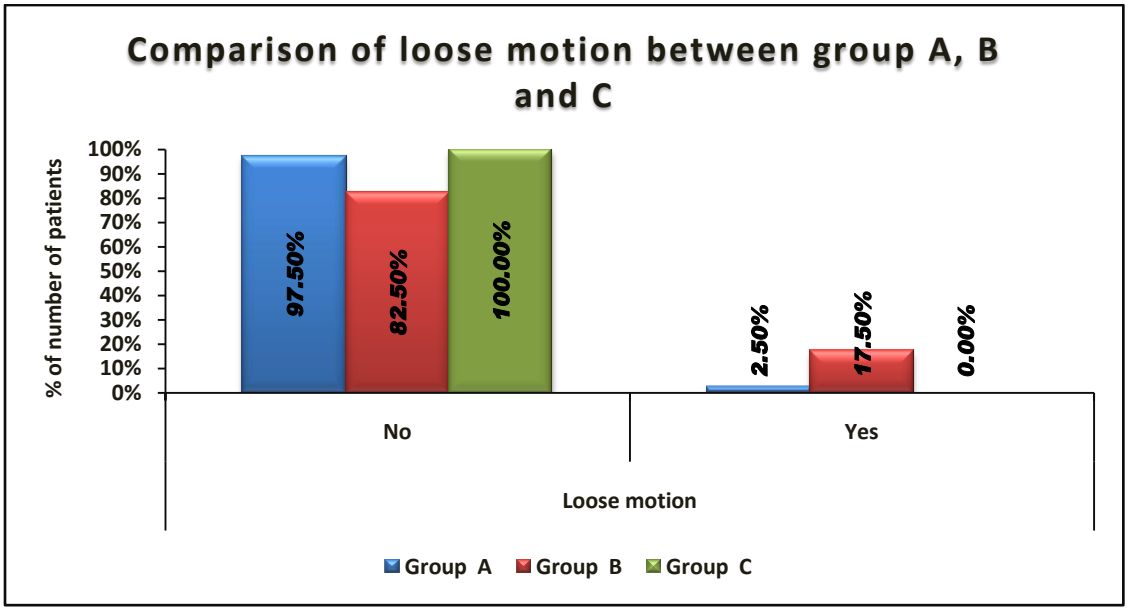

Figure 14: -Comparison of loose motion between group A, B and C.

Proportion of patients with loose motion was significantly higher in group B as compared to group C. (17.50% vs 0% respectively, p value=0.012). Distribution of loose motion was comparable between group A and C (p value=1) as shown in table 14, figure 14.

Table 15: -Comparison of Abdominal Cramps between group A, B and C.

Abdominal cramps	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
No	1 (2.50%)	40 (100%)	0 (0%)	<.0001* A vs B:<.0001* A vs C:0.546* B vs C:<.0001*
Mild/moderate	32 (80%)	0 (0%)	35 (87.50%)	
Severe	7 (17.50%)	0 (0%)	5 (12.50%)	
Total	40 (100%)	40 (100%)	40 (100%)	

* **Fisher's exact test**

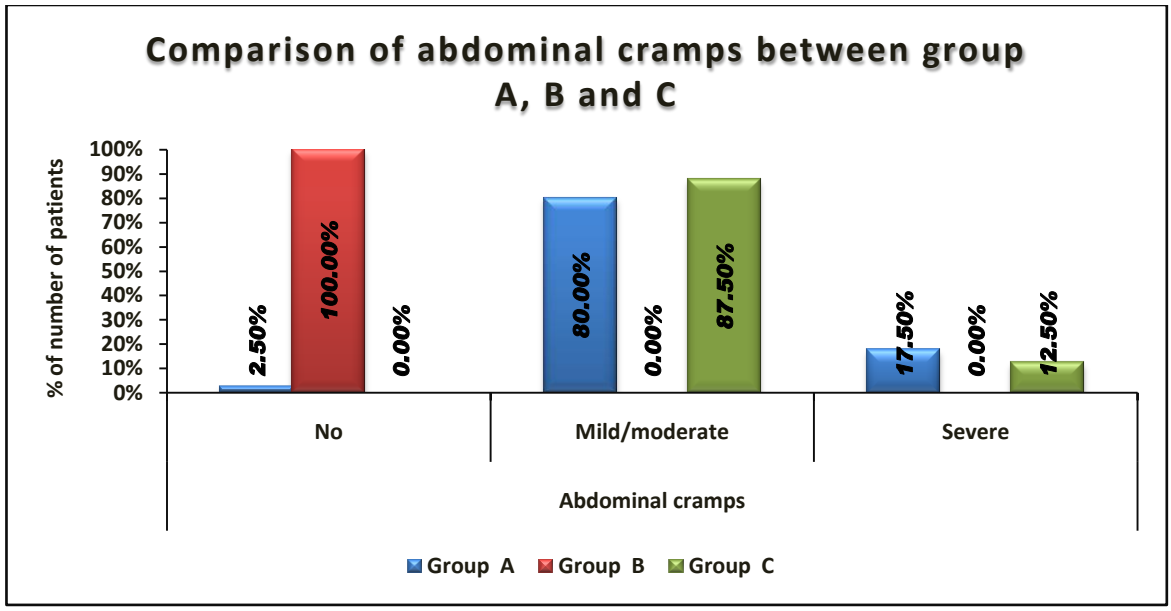

Figure 15: -Comparison of Abdominal Cramps between group A, B and C.

Proportion of patients with mild/moderate and severe abdominal cramps was significantly higher in group A and group C as compared to group B. (Mild/moderate: - 80%, 87.50% vs 0% respectively, Severe: - 17.50%, 12.50% vs 0% respectively). Proportion of patients without abdominal cramps was significantly higher in group B as compared to group A (p value<.0001) and group C (p value<.0001). (100% vs 2.50%, 0% respectively).

Distribution of abdominal cramps was comparable between group A and C. (p value=0.546) as shown in table 15, figure 15.

Table 16: -Comparison of Fever between group A, B and C.

Fever	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
No	30 (75%)	37 (92.50%)	22 (55%)	0.0006† A vs B:0.066* A vs C:0.061† B vs C:0.0002*
Yes	10 (25%)	3 (7.50%)	18 (45%)	
Total	40 (100%)	40 (100%)	40 (100%)	

* Fisher's exact test, † Chi square test

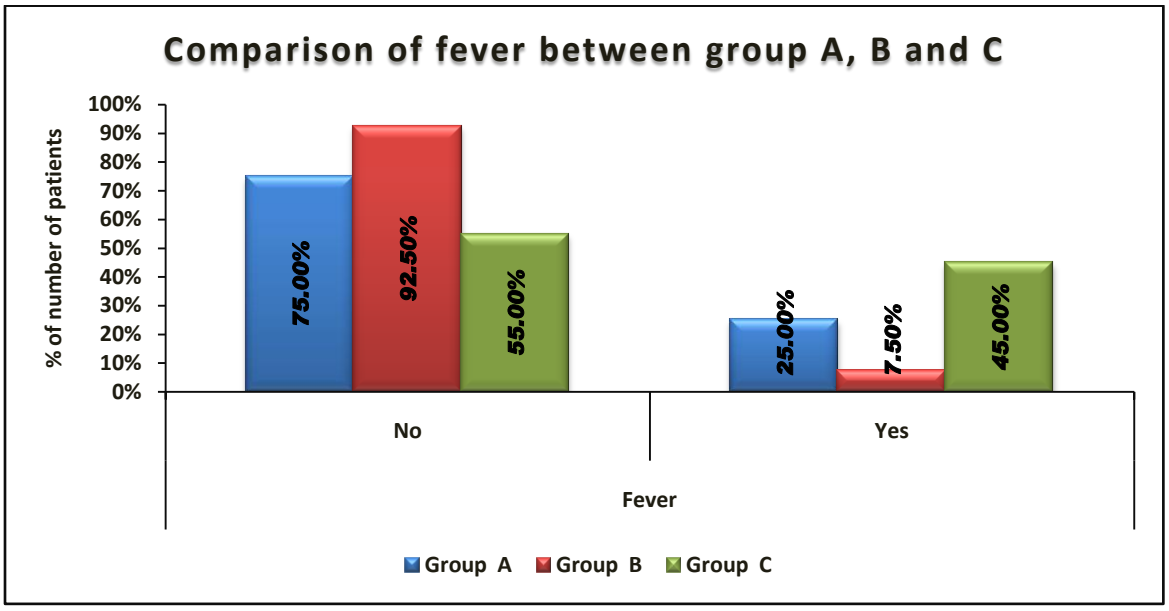

Figure 16: -Comparison of fever between group A, B and C.

Proportion of patients with fever was significantly higher in group C as compared to group B. (45% vs 7.50% respectively). (p value=0.0002)

Distribution of fever was comparable between group A and B (p value=0.066) and between group A and C (p value=0.061).

It is shown in table 16, figure 16.

Table 17: -Comparison of Vaginal Bleeding between group A, B and C.

Vaginal bleeding	Group A(n=40)	Group B(n=40)	Group C(n=40)	P value
Menstrual flow like bleeding	22 (55%)	34 (85%)	20 (50%)	<.0001† A vs B:<.0001* A vs C:0.654† B vs C:<.0001*
Severe bleeding with clots	18 (45%)	6 (15%)	20 (50%)	
Total	40 (100%)	40 (100%)	40 (100%)	

* Fisher's exact test, † Chi square test

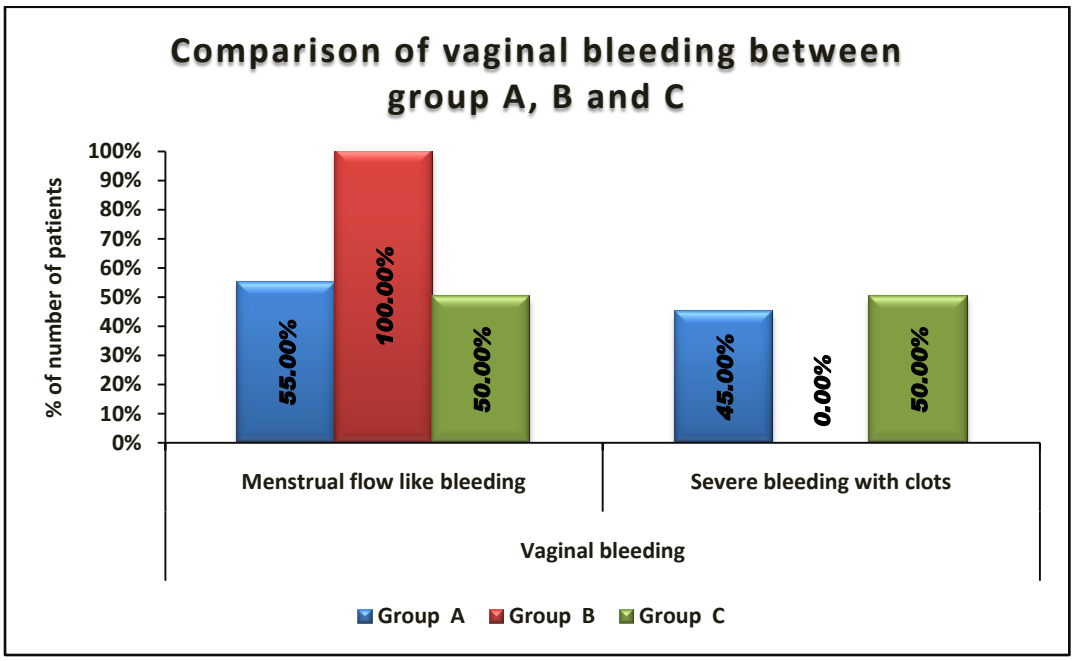

Figure 17: -Comparison of vaginal bleeding between group A, B and C.

Proportion of patients with severe vaginal bleeding with clots was significantly higher in group A and group C as compared to group B. (Severe bleeding with clots: - 45%, 50% vs 15% respectively). Proportion of patients with menstrual flow like vaginal bleeding was significantly higher in group B as compared to group A (p value<.0001) and group C (p value<.0001). (Menstrual flow like bleeding: - 85% vs 55%, 50% respectively) [10].

Distribution of vaginal bleeding was comparable between group A and C. (p value=0.654) It is shown in table 17, figure 17.

Table 18:-Comparison of post-operative side effects between sub lingual, oral and vaginal route.

Post-operative side effects	Group A(n=40)	Group B(n=40)	Group C(n=40)	Total
Vomiting	3 (7.50%)	3 (7.50%)	0 (0%)	6 (5%)
Loose motion	1 (2.50%)	7 (17.50%)	0 (0%)	8 (6.67%)
Abdominal cramps	39 (97.50%)	0 (0%)	40 (100%)	79 (65.83%)
Fever	10 (25%)	3 (7.50%)	18 (45%)	31 (25.83%)
Vaginal bleeding	18 (45%)	0 (0%)	20 (50%)	38 (31.67%)

*** Fisher's exact test, † Chi square test**

DISCUSSION

DISCUSSION

WHO has recommended easy and safe procedures for carrying out abortion at appropriate duration of pregnancy by skilled surgeon, still only about 50% of the abortions are done according to WHO guidelines. In India MTP Act was implemented in 1972, still unsafe abortion is rampant and lakhs of women are hospitalised every year with complications due to illegal abortions.

Different methods are available for first trimester abortion, among them most used are pharmacological and surgical methods. Often surgical methods result in genital tract, especially cervical injuries as cervical dilatation is an integral step of 1st trimester surgical abortions. These injuries can be minimised by cervical ripening prior to surgical abortion. Cervical ripening also reduces operative time, intra-operative blood loss and increases operative ease for the surgeon.

WHO has approved misoprostol for cervical ripening in the year 2003, it can be administered by different routes like oral, sub lingual, vaginal, buccal and rectal.

Misoprostol is prostaglandin of choice as it is economical and constant at room temperature and available in different dosage forms. Misoprostol binds to myometrial cells causing strong myometrial contractions leading to softening and dilatation of cervix. This results in separation of conceptus from uterus thereby initiating abortion process before suction and evacuation [9].

Cervical dilatation is an important aspect as most of cervical injuries and uterine perforation are due to forceful dilatation of cervix. Adequate cervical dilatation decreases pain and facilitates an uncomplicated procedure. Previously osmotic dilator like laminaria were used for cervical ripening. Now a days misoprostol (prostaglandin E1 analogue) is widely prescribed for cervical ripening in labour induction and termination of pregnancy in first trimester.

In our study we have compared the efficacy and acceptance of misoprostol for cervical ripening by different routes before first trimester surgical abortion.

DEMOGRAPHIC CHARACTERISTICS OF STUDY GROUP

Total of 120 patients are included in the study, with 40 in each in group (sublingual, oral and vaginal).

AGE

The mean age among the three groups is compared with other studies.

COMPARISON OF MEAN AGE IN DIFFERENT STUDIES						
Author	**Year**	**N**	**Oral**	**Vaginal**	**Sub-Lingual**	**P Value**
Present Study	2021	120	25.5 ± 4.09	25.5 ± 3.77	25.9 ± 4.94	0.80
A Punyashthira	2014	80	32.1± 6.3	-	30.6 ± 6.0	0.31
Jayati Nath	2013	120	-	26.2	36	>0.05
S Parveen	2010	150	27.3 ± 5.4	26.8 ± 5.4	27.7 ± 5.0	>0.05
P Saxena	2008	200	25.6 ± 2.5	26.8 ± 3.4	26.6 ± 2.2	>0.05
L Cakir	2004	160	29.9 ± 6.4	30.9 ± 6.09	-	>0.05

In current study among the 120 patients, mean age in oral group is 25.5 ± 4.09 years. Mean age in Vaginal group is 25.5 ± 3.77 yrs. Mean age in Sub-lingual group is 25.9 ± 4.94 years.

p value is 0.6 which is not significant.

In study by S Parveen et al, oral group mean age is 27.3 ± 5.4 yrs. Vaginal group mean age is 26.8 ± 5.4 yrs. Sub-lingual mean age is 27.7 ± 5.0 yrs. There is no significant difference seen in mean age distribution [57].

In study by P Saxena et al, oral group mean age is 25.6 ± 2.5 yrs. Vaginal group mean age is 26.8 ± 3.4 yrs. Sub lingual group mean age is 26.6 ± 2.2 yrs , with no significant difference in age distribution [16].

As evident from the above table, mean age in most of the studies showed similar results with no statistical significance.

RELIGION AND RESIDENCE

In the present study Majority of the women 56.6% were Muslims, whereas in the study by Saxena majority were Hindu.

In the present study women residing in rural area were 19.1% and urban are 80%. It affirms majority are from urban region.

LITERACY

Very few studies have described about education of women. In the present study 20% of women were illiterate, 48.3% had primary school education, 23.3% had secondary school education and 9.1% were graduates. In study done by Awassada P, 7% were illiterates, and majority i.e 52% were graduates [35].

PARITY

Mean Parity						
Author	**Year**	**N**	**Oral**	**Vaginal**	**Sub-Lingual**	**P Value**
Present Study	2021	120	2.5 ±1.2	3.1 ±2.3	1.8±1.3	NS
Varsha Kotwal	2019	120	2.59 ± 1.30	3.01 ± 0.98		NS= 0.078
Jayati Nath	2013	120		1.35 ± 0.75	1.15 ± 0.75	NS = 0.15
S Parveen	2010	150	1.2 ± 1.2	0.9 ± 1.0	1.4 ± 1.2	NS =0.200
P Saxena	2008	200	3.3 ± 2	3.5 ± 2.0	3.5 ± 2	NS

The obstetrical profile of patients in all three groups was comparable with other studies.

GESTATIONAL AGE

Gestational Age						
Author	**Year**	**N**	**Oral**	**Vaginal**	**Sub-Lingual**	**P Value**
Present Study	2021	120	12.24 ± 2.05	10.7 ± 2.5	10.71 ± 1.3	NS (<0.005)
A Punyashthira	2014	80	9.8±1.4		10.1± 1.4	NS
Jayati Nath	2013	120		8.37± 2.7	8.3± 2.8	NS
S Parveen	2010	150	8.5±1.4	8.2±1.8	9.2± 2.8	NS
P Saxena	2008	200	8.4±2.3	8±4.2	7.9± 0.8	NS

In our study mean gestational age in sub lingual group is 10.71 ± 1.3weeks, mean gestational age in oral group is 12.24 ± 2.05 weeks and mean gestational age in vaginal group is 10.7 ± 2.5 weeks. p value is <0.005 which is not statistically significant.

Similarly, nostatistically significant difference in gestational age was seen in other studies.

PRIMARY OUTCOMES

A) MEAN CERVICAL DILATATION

Mean Cervical Dilatation (mm)						
Author	**Year**	**N**	**Oral**	**Vaginal**	**Sub-Lingual**	**P Value**
Present Study	2021	120	6.2 ±1.2	8.1 ± 0.6	9.2 ±1.5	S <0.002
Divya Sinha	2017	150	2.6±4.8	8.4±5.2	9.3±5.8	S (<0.001)
A Punyashthira	2014	80	5.7±1.5		7.1±1.1	S(<0.001)
Jayati Nath	2013	120		6.9 ± 0.796	7.76 ± 1.35	S(<0.001)
S Parveen	2010	150	4.8 ± 5.1	8.1 ± 5.4	9.1 ± 5.8	S(<0.001)
P Saxena	2008	200	8.2 ± 2.6	7.6 ± 2.6	9.9 ± 2.1	S (<0.001)

In present study, cervical dilatation before the procedure was measured with Hegar's dilator as 5mm, 5-8mm, >8mm. The mean cervical dilatation was significantly higher in sublingual group followed by vaginaland oralgroups (9.2±1.5, 8.1 ± 0.6and 6.2 ±1.2mm respectively) (p <0.002). Similar results were obtained in other studies also.

In Primigravida patients there is no significant difference in cervical dilatation in vaginal, oral and sub lingual groups with p value > 0.005. In multi gravida patients there is

significant difference in sublingual and oral route mainly in patients with previous history of normal vaginal delivery.

p value <0.004 which is significant.

In study done by DSinha et al, mean cervical dilatation was 2.6±4.8 mm in oral group, 8.4±5.2 mm in vaginal group and 9.3±5.8 mm in sub lingual group, p value <0.001 which shows significant difference between sublingual and oral route of administration. It required additional mechanical means of cervical dilatation in oral group [57].

In study by A. Punyashthira et al, mean cervical dilatation was 7.1±1.1 mm in sub lingual group compared to 5.7±1.5mm in oral group. p value was <0.001 which is statistically significant [16].

In study by JNath et al, mean cervical dilatation was 7.76 ± 1.35mm in sub lingual group and 6.9 ± 0.796 mm in vaginal group, p value <0.001 which is statistically significant [34].

In study by S Parveen, mean cervical dilatation in sublingual, vaginal, oral route was 9.1 ± 5.8 mm, 8.1±5.4 mm and 4.8±5.1 mm respectively. P value <0.002, which is significant [33].

In study done by P Saxena , mean cervical dilatation in sub lingual group is 9.9± 2.1mm, In vaginal group is 7.6± 2.6 mm, and in oral route is 8.2± 2.6 mm. P value is <0.002 which is significant [16].

It is observed in all studies that sublingual route is more effective than oral and vaginal route for adequate cervical dilatation before surgical abortion.This result is probably due to different absorption and pharmacokinetics of Misoprotol when given through different routes. Zieman et al reported in their study that, systemic bioavailability of misoprostol was three times higher after vaginal administration than after oral administration. The probable reason for this observation is that, plasma level is long lasting and progressively increasing after prolonged contact with vaginal mucosa which is very vascular. However, there are large individual variations and inconsistency in drug absorption through the vaginal mucosa. At times small unabsorbed pieces of tablet are found in vagina at the time of surgical procedure, hours after its administration. Hence vaginal route may not be the ideal route of administration. Another way of rapid absorption of misoprostol is through the vascular buccal mucosa [16]. Tang et al compared the pharmacokinetics of misoprostol by sublingual, oral and vaginal route with the addition of water and found that time

required to reach peak serum concentration was least with sublingual misoprostol. It also achieved significantly higher peak serum concentrations and showed the greatest bioavailability when compared to other routes [11] [12].

B) DURATION OF PROCEDURE

Duration of Procedure (minutes)						
Author	**Year**	**N**	**Oral**	**Vaginal**	**Sub-Lingual**	**P Value**
Present Study	2021	120	10.25±4.32	9.88±3.84	8.12 ±3.14	S (<0.001)
Divya Sinha	2017	150		8.8±5.4	7.0±3.6	S (<0.001)
A Punyashthira	2014	80	7.3±4.6		5.2±3.3	S (<0.02)
Jayati Nath	2013	120		9.65 ± 1.2	7.36 ± 1.60	S (<0.001)
S Parveen	2010	150	10.6 ± 5.6	12.7 ± 5.8	8 ± 3.5	S (<0.001)
P Saxena	2008	200	4.9 ± 1.7	5.2 ± 1.8	3.6 ± 1.0	S (<0.01)

In the present study procedure time was least in sublingual group with a mean of min 8.12±3.14, mean time for vaginal group was 9.88±3.84 min and 10.25±4.32 min for oral route, p value is < 0.001 which is statistically significant and can be explained on the basis of better cervical ripening and dilatation achieved in sublingual group.

In study by D Sinha et al, the mean duration of procedure was 7.0±3.6 min in sublingual route, 8.8±5.4 min in vaginal route, 14.7±5.1 min in oral route. p value <0.02 which is significant [43].

In study by A Punyashthira et al, the mean duration of procedure in sublingual route was 5.2±3.3 min and7.3±4.6 min in oral route. p value <0.003 which is statistically significant [18].

In study by J Nath et al, the mean duration of procedure in sublingual route is 7.36 ± 1.60 min and in vaginal route is 9.65 ± 1.2 min. P value< 0.003 which is significant [34].

In the study by S Parveen et al, the mean duration of procedure in sub lingual route is 8 ± 3.5min, in vaginal route is 12.7 ± 5.8 min and oral route is 10.6 ± 5.6 min. p value is <0.001 which is statistically significant [33].

In the study by P Saxena et al, the mean duration of procedure in oral route is 3.6 ± 1.0 min, in vaginal route is 5.2 ± 1.8 min, in oral route is 4.9 ± 1.7min. p value is <0.01 which is statistically significant [16].

C) INTRA OPERATIVE BLOOD LOSS

Intra Operative Blood Loss (ml)						
Author	**Year**	**N**	**Oral**	**Vaginal**	**Sub-Lingual**	**P Value**
Present Study	2021	120	20.2 ±4.4	25.4±5.02	30.3 ±3.42	S(<0.002)
Divya Sinha	2017	150	18.8±9.5	23.4±15.7	25.8±18.6	S(0.065)
A Punyashthira	2014	80	17.9±8.6		17.4±7.4	NS
Jayati Nath	2013	120		24.87 ± 3.04	24.07 ± 2.02	NS
S Parveen	2010	150	18.0 ± 8.8	17.7 ± 7.2	23.4 ± 17.4	S(<0.004)
P Saxena	2008	200	17.7 ± 7.3	16.9 ± 7.0	17.9 ± 6.3	NS

In present study, intra operative blood loss was more in sublingual route compared to oral and vaginal route.

In study by DSinha, maximum amount of blood loss was seen in sublingual route with mean 25.8±18.6 ml, 23.4±15.7 ml in vaginal route, 18.8±9.5 ml in oral route. with p value <0.003 which is statistically significant [43].

In study by A Punyashthira, amount of blood loss in oral route is 17.9±8.6 ml compared to 17.4±7.4 ml in sub lingual route. p value is 0.78 which is not significant [18].

In study by JNath, mean amount of blood loss in sub lingual route 24.07 ± 2.02 ml, vaginal route is 24.87 ± 3.04 ml. p value >0.005 which is not significant [34].

In study by S Parveen, mean amount of blood loss in sub lingual route is 23.4 ± 17.4 ml, vaginal route is 17.7 ± 7.2 ml, oral route is 18.0 ± 8.8 ml. p value is <0.003 which is significant [33].

In study by P Saxena, mean amount of blood loss in sub lingual route is 17.9 ± 6.3ml, vaginal route is 16.9 ± 7.0 ml, oral route is 17.7 ± 7.3 ml. p value is >0.005 which is not significant [16].

Outcome from my study was similar to the studies done by D Sinha, S Parveen, showing minimum amount of blood loss is when misoprostol is administrated by oral route [43].

SECONDARY OUTCOMES

a) **PAIN**

In present study most of the patients experienced abdominal pain and lower back pain after taking misoprostol. In patients who received sub lingual misoprostol 32 (80%) had moderate pain, 7 (17.5%) had severe pain. In patients with vaginal route, 35 (87.5%) had moderate pain, 5 (12.5%) had severe pain. NSAIDs were given to decrease the pain.

In present study 88.4% of the primigravida patients experienced more pain in sub lingual group compared to vaginal group. Among second gravida patients, 46% experienced maximum pain on taking misoprostol by sublingual route. Among third gravida patients, 38% experienced maximum pain by sublingual route compared to vaginal and oral route.

Similar results were obtained in study done by Saxena et al, where pain was more in sublingual than in oral group (p value<0.05) [16].

According to P Kaur et al pain was more in sub lingual group compared to vaginal group

(p value <0.004) [26].

According to Vimala et al, pain was more in patients who received sub lingual misoprostol [22].

The present study does not co relate with study done by S Parveen, where pain was more in vaginal group than in oral and sublingual group [33].

B**) VOMITING**

In present study nausea was observed in most of the patients, vomiting was reported by 7% patients in sublingual group and 7.5% patients in oral group. As nausea and vomiting were self-limiting, no specific treatment was required.

Present studied is supported by Saxena et al, Sinha et al, Vimala et al. In all studies p value >0.005, so it is not significant between different regimens [16].

C) **DIARRHOEA**

In present study diarrhoea was reported by 17.5% patients in oral group and 2.5% in sub lingual group, which is not statistically significant>0.005.

Study by Sharma M et al shows that diarrhoea is more common in sub lingual group than vaginal group [22].

In study by K Parneet et al no patients reported diarrhoea.

D**) FEVER**

Prostaglandin's are produced in body in reaction to tissue damage causing fever.

In present study 45% of patients in vaginal group had fever, 25% in sub lingual group and 7.5% in oral group had fever. This shows fever is seen more in vaginal group than others

In study by P Saxena, 8 % in sub lingual group had fever, 6% in oral group and, 2 % in vaginal group had fever, which is not similar to present study [16].

In study by D Sinha, fever was reported in 6% of sub lingual and 2 % oral groups [43].

E) **VAGINAL BLEEDING**

In present study heavy bleeding associated with clots is seen in sublingual (45%) and vaginal group (50%) compared to oral group which is significant with p value (0.001). Menstrual like flow bleeding was commonly seen in oral group compared with sublingual and vaginal group. In our study amount of bleeding increased with increase in parity.

Studies done by Sharma et al and Vimala et al observed that amount of blood loss is more in sub lingual group [22].

P Kaur et al compared sub lingual and vaginal misoprostol and found that vaginal bleeding is more in sub lingual group compared to vaginal group [47].

F) **ACCEPTABILITY OF THE REGIMEN**

In present study sublingual route (80%) is more acceptable than vaginal route (40%), as it is easy and more convenient.

Most of the patients accepted sub lingual route as it is easily administered. Some of the patients felt that sub lingual route is not convenient as it has unpleasant taste.

The present study is also supported by N Sharma et al, Vimala et al, who found sub lingual tablet is more convenient to take than vaginal [26].

SUMMARY

SUMMARY

This Prospective Randomised Non blind study was conducted in department of Obstetrics and Gynaecology, Santosh Medical Hospital, Ghaziabad. The aim of the study was to compare the efficacy and tolerability of sublingual, oral and vaginal Misoprostol for cervical ripening before first trimester surgical abortion and to observe the most effective route of administration.

Approval was obtained from the Ethics committee and consent was taken from each patient.

Women with singleton intrauterine pregnancy up to 12 weeks of gestation, who gave consent for surgical abortion, were included. Any women with multiple pregnancy, history of allergy to prostaglandin, severe anaemia, renal and cardiac disease were excluded.

A detailed history was taken including menstrual history and obstetric history. A thorough general physical examination (specially to check for anaemia), systemic examination to rule out cardiovascular and respiratory problems and bimanual per vaginal examination was done in all patients [6].

Various investigations like haemoglobin, blood group & Rhesus typing, urine routine &microscopy and ultrasound pelvis were done.

All the women were counselled regarding various methods of contraception with their advantages and disadvantages and were given options to decide which suits them and to support them in solving any problems that may arise with the selected method.

Total of 120 subjects were taken in the study who visited OPD. After randomisation patients were allocated into three group with 40 patients in each group. The patients were given 400mcg of misoprostol by three different routes (oral, vaginal, sub lingual) 4 hrs before the suction and evacuation.

The groups allocated were Group A: Sub-Lingual, Group B: Oral, Group C: Vaginal

Pre-operatively during the waiting time they were observed for abdominal pain, vaginal bleeding, vomiting, diarrhoea, and fever.

Data obtained was analysed by ANOVA and Chi- Square Test. P value<0.005 is considered statistically significant.

The socio demographic profile of the three groups did not show any significant difference in the outcome of the study. The mean age in the three groups was around 25.5 ± 4.09. The distribution by socioeconomic status in the three groups were comparable with p value =0.41.

Majority of the patients 68% had received primary & secondary education and 20% were illiterate.

Majority of the patients had onset of bleeding within 2-3 hrs of intake of misoprostol. There is no significant difference, which shows all three regimens have similar efficacy in initiating the process of abortion.

In sub lingual group 100% patients had maximum cervical dilation with no need for mechanical dilatation. Satisfactory dilatation was observed in vaginal group compared to oral group. In 30% of patients belonging to oral group dilatation was very less compared to vaginal and sublingual groups. The efficacy of the drug to cause maximum cervical dilatation was seen when drug was given by sub lingual route than vaginal and oral route.

The mean size of Hegar's dilator to pass through os without any resistance is 11.4±1.89 in sublingual group, 12.85±2.67in vaginal group and 10.4±1.90in oral group. Among the three-dose regimen, sublingual misoprostol 400µg causes more dilatation than oral and vaginal groups. p value=0.001

The Duration of procedure was less in sub lingual group than vaginal and oral group, which is due to misoprostol taken in sublingual route has better bioavailability and different absorption kinetics compared to vaginal and oral routes.

The mean intra operative blood loss was less in oral route with mean 20.2 ± 4.4 ml, than vaginal and sublingual route.

The side effects like vaginal bleeding, diarrhoea and fever were more in vaginal and oral route. severe abdominal cramps and vomiting was seen in sub lingual group. After the procedure, post operative analgesic for 3days and antibiotic for 5 days was prescribed. Follow up after 10 days or a month was advised and none of them had any major complaints.

Significant differences in the above study did not have the potential to cause extreme clinical improvements except decrease in the number of patients requiring added cervical

dilatation. Reducing the need for cervical dilatation will decrease the number of complications like cervical and uterine injuries.

Sub lingual route of administration and oral route were preferred in majority of them due to the convenience.

CONCLUSION

CONCLUSION

Misoprostol is the drug of choice for cervical priming before abortion, as it is long lasting and increasing levels of doses are not required as in case of medical abortion.

From our study it is concluded that sublingual route of administration of 400 µg misoprostol for cervical ripening 4 hours before surgical abortion is preferable when compared to oral and vaginal route. Cervical dilatation was maximum with tablet Misoprostol administered by sublingual route with reduced use of mechanical dilatation. The duration of procedure was shorter, and most importantly it is preferred route by majority of patients, though it has bitter taste, nausea, and vomiting. Sublingual route has high systemic concentration due to avoidance of first pass metabolism resulting in favourable results. Vaginal route is also effective due to its slow and constant absorption through the vaginal mucosa. Discomfort associated with its administration limits its universal acceptance in clinical practice.

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ANNEXURES

PATIENT INFORMATION SHEET

NAME:

AGE:

ADDRESS:

REGISTRATION NUMBER:

OCCUPATION:

PHONE NUMBER:

CHIEF COMPLAINTS:

PROVISIONAL DIAGNOSIS:

CASE PERFORMA

Patient's Name:

Age:

Education:

Address & phone no:

Socioeconomic Status:

- Menstrual history:

  LMP- PMH-

- Obstetrics history:

  Married life- G P L A-

- Contraceptive History:
- History of present pregnancy:
  - Fever
  - Cold/cough
  - Burning micturition
  - Constipation
  - Tuberculosis
  - Weight gain
  - Heat intolerance
  - Drugs
  - Any Addiction

- History of present illness

- History of past illness
  1. Surgical
  2. Medical

- Personal History
- Family History
- Socio-economic History

PHYSICAL EXAMINATION

- General Condition
  - Weight: Height: BMI:
  - Pallor Cyanosis
  - Icterus Lymphadenopathy
  - Clubbing Oedema
- Vitals
  - BP
  - PR
  - Respiratory rate
  - Temperature
- P/A
- P/S
- P/V

INVESTIGATIONS

- CBC
- Urine routine and microscopy
- Blood grouping/Rh Typing
- VDRL
- HIV/Hbs Ag
- HCV
- Mantoux test
- Sr TSH
- RBS
- Pelvic Ultrasound
- Any other

INFORMED CONSENT

NAME OF THE GUIDE:

NAME OF THE PATIENT:

AGE:

ADDRESS:

PHONE NUMBER:

S.NO: DATE:

I have been explained the details of the study entitled **"A COMPARATIVE STUDY OF SUB LINGUAL, VAGINAL, ORAL MISOPROSTOL IN CERVICAL RIPENING FOR FIRST TRIMESTER ABORTION"** and my questions regarding the study have been answered to my satisfaction in a language understood by me.

1. I understand that I have the right to withdraw from the study at any time and to decline to answer any particular question.

2. I understand that my participation in this study is confidential and that no material that could identify me will be used in the analysis and in any reports based on this study.

I hereby provide my consent in the study entitled "**A COMPARATIVE STUDY OF SUB LINGUAL, VAGINAL, ORAL MISOPROSTOL IN CERVICAL RIPENING FOR FIRST TRIMESTER ABORTION**".

signature /thumb impression of the patient

signature / thumb impression of the witness

<u>सूचित सहमति</u>

गाइड का नाम: -

रोगी का नाम:

आयु:

पता: -

फ़ोन नंबर:-

एस एन ओ :

मुझे अध्ययन के विवरण समझाया गया है & “पहली तिमाही में गर्भपात केअ धीन, योनि, मौखिक मिसो प्रोस्टोल की तुलना". मेरा अध्ययन के बारे में प्रश्नों को एक मेरे द्वारा समझा भाषा में मेरी संतुष्टि का उत्तर दिया गया

1. मैं समझता हूं कि मुझे किसी भी समय अध्ययन सेवा पस लेने का अधिकार है और किसी विशेष प्रश्न का उत्तर देने में गिरावट आई है।

2. मैं समझता हूं कि इस अध्ययन में मेरी भागीदारी गोपनीय है और कती है और रिपोर्टइस अध्ययन के आधार पर किसी भी में विश्लेषण उपयोग नहीं की जाएगी।

मैं इस प्रकार अध्ययन में अपनी सहमति प्रदान करता हूं “पहली तिमाही में गर्भपात के अधीन, योनि, मौखिक मिसो प्रोस्टोल की तुलना"

रोगी के हस्ताक्षर / अंगूठे की छाप

गवाह के हस्ताक्षर / अंगूठे की छाप

ETHICAL COMMITTEE CLEARANCE

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

F. No. SU/2021/1830[57] Dated: 17.07.2021

Subject: Grant of Ethical Clearance for Thesis Protocol Topic "**A COMPARATIVE STUDY OF SUBLINGUAL , VAGINAL AND ORAL MISOPROSTOL IN CERVICAL RIPENING FOR FIRST TRIMESTER ABORTION",** submitted by **Dr. Pilla Sadhana,** MD/MS student of Batch 2020-2021, Department of **Obstetrics & Gynaecology**.

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With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled **"A COMPARATIVE STUDY OF SUBLINGUAL , VAGINAL AND ORAL MISOPROSTOL IN CERVICAL RIPENING FOR FIRST TRIMESTER ABORTION", Dr. Pilla Sadhana** is informed that the Thesis Protocol submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital in its meetings held on 19.03.2021, 22.03.2021, 24.03.2021, 25.03.2021, 26.03.2021, 27.03.2021 and 06.04.2021. The recommendations of the **Screening Committee** were considered in detail by the Institutional **Ethics Committee** in its meeting held on **12.07.2021** and the same was **approved** by the **Ethics Committee**.

He /She is informed accordingly for further necessary action.

[Dr. V. P. Gupta]
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S/L	Sl.No	Age	RELIGION	LOCALITY	EDUCATION	Parity	Period of Gestation (Weeks)	mparision of Different Paramet Cevical Dilatation	Duration of Procedure	Intra Operative Blood Loss	Adverse Effects Vomiting	Loose Motion	Abdominal Cramps	Fever	Vaginal Bleeding
Group A	1	22	2	1	1	g2p1l1	7	2	15min	1	0	0	1	1	2
	2	24	2	1	1	primi	6+3	2	20	1	0	0	1	0	2
	3	19	2	1	2	primi	8	2	25	1	0	1	1	0	2
	4	25	1	1	2	G3P1L1A1	8+4	2	15	1	1	0	1	1	2
	5	26	1	1	3	G2P1L1	9	2	20	2	0	0	0	0	1
	6	23	2	1	1	G2P1L1	10	2	15	1	0	0	1	0	1
	7	24	1	2	0	G3P1L1A1	8+2	2	20	1	0	0	1	0	2
	8	26	1	1	1	PRIMI	7	2	15	1	0	0	1	1	1
	9	28	2	1	3	G2A1	11	2	20	1	0	0	1	0	1
	10	29	2	1	1	G3P2L2	10+2	2	25	1	0	0	1	0	2
	11	22	1	1	2	G3A2	7	2	20	1	0	0	1	0	1
	12	27	2	1	1	G4PILIA2	10	2	20	1	0	0	1	0	1
	13	24	1	1	1	PRIMI	8	2	20	1	0	0	1	1	1
	14	32	2	1	1	G3P2L2	9+4	2	20	1	0	0	1	0	1
	15	36	2	2	2	G4P2L2A1	11	2	25	1	0	0	1	1	2
	16	27	1	2	0	G2P1L1	14	2	20	1	0	0	2	0	2
	17	34	1	1	1	G3P1L1A1	12	2	15	1	0	0	1	1	1
	18	22	2	1	0	PRIMI	12+5	2	15	1	0	0	1	0	2
	19	36	1	1	3	G2P1L1	14	2	20	1	0	0	1	0	1
	20	21	2	1	2	PRIMI	9+4	2	15	1	0	0	1	0	1
	21	23	2	1	1	G2P1L1	11	2	20	1	0	0	1	0	1
	22	27	1	1	1	G2A1	12	2	2	1	1	0	2	1	2
	23	29	2	2	0	G3P1L1A1	14+5	2	20	1	0	0	2	0	2
	24	37	2	1	1	G5P3L3A1	14	2	15	1	0	0	1	0	2
	25	36	1	1	1	G3P1L1A1	12+4	2	20	1	0	0	1	0	2
	26	32	2	1	0	G2P1L1	11	2	15	1	0	0	1	0	1
	27	27	3	1	1	PRIMI	10	2	20	1	0	0	1	0	1
	28	19	1	1	1	PRIMI	9	2	15	1	0	0	1	0	1
	29	21	1	2	0	G2P1L1	10+4	2	15	1	0	0	2	0	2
	30	22	1	1	2	PRIMI	11	2	15	1	0	0	1	1	1
	31	26	2	1	1	PRIMI	9	2	15	1	0	0	1	0	1
	32	24	1	2	0	PRIMI	10	2	15	1	0	0	1	0	1
	33	27	2	1	2	G2P1L1	9+4	2	15	1	0	0	2	0	1
	34	26	2	1	1	G2P1L1	12	2	15	1	0	0	1	0	1
	35	24	2	1	2	PRIMI	12+6	2	20	1	0	0	1	0	2
	36	21	2	1	1	PRIMI	14	2	15	1	0	0	2	0	2
	37	19	1	1	1	PRIMI	14	2	15	1	0	0	1	1	2
	38	20	2	1	0	G2A1	12	2	20	1	0	0	1	0	1
	39	28	3	1	2	G2P1L1	12+4	2	20	1	1	0	1	0	2
	40	24	1	1	3	G2P1L1	13	2	20	1	0	0	2	1	1

	Sl.No						Period of Gestation	mparision of Different Paramet			Adverse Effects				
ORAL		Age	RELIGION	LOCALITY	EDUCATION	Parity	(Weeks)	Cevical Dilatation	Duration of Procedure	Intra Operative Blood Loss	Vomiting	Loose Motion	Abdominal Cramps	Fever	Vaginal Bleeding
Group B	1	22	2	1	1	PRIMI	9	0	30	1	0	0	0	0	1
	2	23	2	1	1	G2P1L1	10+2	1	25	1	0	0	0	0	1
	3	25	2	2	0	PRIMI	12	0	30	1	1	0	0	0	1
	4	24	2	1	2	G2P1L1	11	1	20	1	0	0	0	0	1
	5	32	2	2	0	G3P1L1A1	13+1	1	25	1	0	0	0	0	1
	6	27	1	1	3	G3P2L2	14	1	20	1	0	1	0	0	1
	7	29	2	1	1	G2P1L1	12	1	25	1	0	0	0	0	1
	8	31	1	1	2	G3P2L2	8+5	1	25	1	0	0	0	0	1
	9	24	3	1	1	PRMI	9+3	0	30	1	0	1	0	0	1
	10	26	1	1	2	G2A1	10	0	30	1	0	0	0	0	1
	11	26	2	2	0	G2P1L1	15+3	1	25	1	0	0	0	0	1
	12	29	2	1	1	G4P1L1A2	14	1	25	1	0	0	0	0	1
	13	22	2	1	1	G2P1L1	9+6	1	20	1	0	0	0	0	1
	14	21	2	1	1	PRIMI	7+5	0	20	1	0	0	0	0	1
	15	19	1	1	2	PRIMI	10	0	20		0	1	0	0	1
	16	22	2	1	2	G2P1L1	12+5	1	15	1	0	0	0	0	1
	17	26	1	1	1	PRIMI	14+4	0	20	1	1	0	0	0	1
	18	24	2	2	1	G2P1L1	15+1	1	15	1	0	0	0	0	1
	19	26	2	1	2	G3P1L1A1	14+4	1	15	1	0	0	0	0	1
	20	21	2	1	1	PRIMI	12	0	20	1	0	1	0	0	1
	21	22	1	1	1	G3P2L2	11+4	1	25	1	0	0	0	1	1
	22	26	1	1	1	PRIMI	10+3	0	20	1	0	0	0	0	1
	23	25	2	2	0	G2P1L1	14	1	20	1	0	0	0	0	1
	24	22	2	1	3	PRIMI	15+4	0	25	1	0	0	0	0	1
	25	27	1	1	0	G3P1L1A1	16+1	1	30	2	1	1	0	0	1
	26	32	2	1	1	G3P2L2	13	1	25	1	0	0	0	0	1
	27	29	1	2	0	G2P1L1	12	1	20	1	0	0	0	0	1
	28	30	2	1	2	G4P2L1A1	11+6	1	20	1	0	0	0	1	1
	29	21	2	1	1	PRIMI	12	1	25	1	0	0	0	0	1
	30	18	2	1	1	PRIMI	10+5	0	20	1	0	1	0	0	1
	31	34	1	1	3	G6P3L1A2	11	1	20	1	0	0	0	0	1
	32	23	2	1	2	G2P1L1	14+2	1	25	1	0	0	0	0	1
	33	34	2	2	1	G4P2L1A1	13	1	25	1	0	0	0	0	1
	34	23	1	1	1	PRIMI	12	0	20	1	0	0	0	0	1
	35	32	1	2	0	G4P2L2A1	10+4	1	30	2	0	0	0	0	1
	36	21	1	1	2	PRIMI	13	1	20	1	0	1	0	0	1
	37	24	1	1	2	G2P1L1	15	1	25	1	0	0	0	0	1
	38	25	2	1	0	G2P1L1	13	1	25	1	0	0	0	0	1
	39	26	1	1	1	PRIMI	12	1	30	2	0	0	0	0	1

VAGINAL	Sl.No	Age	RELIGION	LOCALITY	EDUCATION	Parity	Period of Gestation	M			Adverse Effects				
							(Weeks)	Cevical Dilatation	Duration of Procedure	Intra Operative Blood Loss	Vomiting	Loose Motion	Abdominal Cramps	Fever	Vaginal Bleeding
Group C	1	22	2	1	1	PRIMI	10	1	15	2	0	0	1	1	2
	2	24	2	2	0	G2P1L1	11+4	1	20	2	0	0	2	0	2
	3	23	2	1	1	PRIMI	12	1	20	2	0	0	1	1	2
	4	26	2	1	2	G2P1L1	9+5	1	15	1	0	0	1	1	1
	5	32	1	1	1	G3P2L2	12+4	1	15	2	0	0	1	1	2
	6	31	2	2	0	G4P3L3	13+2	1	20	2	0	0	2	1	2
	7	26	2	1	3	G5P2L2A2	11+3	1	20	2	0	0	1	0	2
	8	27	2	1	2	G4P2L2A1	12	1	20	2	0	0	1	1	2
	9	29	1	1	1	G6P3L2A2	14	1	15	1	0	0	1	0	2
	10	30	1	1	2	G3P2L1	11	1	20	2	0	0	1	1	2
	11	19	2	1	1	PRIMI	10+1	1	25	1	0	0	1	1	1
	12	21	2	2	0	PRIMI	10	1	20	2	0	0	2	1	2
	13	22	1	1	1	G2P1L1	11	1	15	1	0	0	1	0	1
	14	25	2	1	1	G3P2L1	13	1	15	1	0	0	1	1	1
	15	27	2	1	2	G3P2L2	11	1	15	1	0	0	1	1.00	1
	16	25	1	1	2	G2P1L1	9+4	1	20	2	0	0	1	0	2
	17	28	2	2	0	G4P2LL1A1	11	1	20	2	0	0	2	0	2
	18	29	1	2	1	G4P1L1A2	12+5	1	25	2	0	0	1	1	2
	19	21	1	1	3	PRIMI	10	0	30	2	0	0	2	0	2
	20	20	1	1	0	PRIMI	11	1	20	1	0	0	1	0	1
	21	19	1	1	1	PRIMI	9+2	1	15	1	0	0	1	1	1
	22	28	2	1	1	G5P2L2A2	11	1	15	1	0	0	1	0	1
	23	30	1	1	1	G4P3L3	8+4	1	20	1	0	0	1	0	1
	24	19	2	1	1	G2P1L1	9	1	20	2	0	0	1	1	1
	25	20	2	2	1	PRIMI	10	0	30	2	0	0	1	1	2
	26	22	1	1	1	G2P1L1	12	1	20	1	0	0	1	0	1
	27	24	2	1	3	G3P1L1A1	12+2	1	20	2	0	0	1	1	1
	28	26	1	1	2	G2P1L1	11+2	1	20	1	0	0	1	0	1
	29	30	2	1	1	G3P2L1	11	1	20	2	0	0	1	1	2
	30	24	2	2	0	G2P1L1	10	1	20	1	0	0	1	0	1
	31	29	1	1	1	G3P2L2	9+4	1	15	1	0	0	1	0	1
	32	28	2	1	1	G2P1L1	11	0	20	2	0	0	1	1	2
	33	27	2	1	2	G4P2L2A1	12	1	20	2	0	0	1	0	1
	34	25	1	1	1	G2P1L1	10	0	20	2	0	0	1	0	2
	35	23	1	1	3	G3P2L2	9+4	0	25	2	0	0	1	0	1
	36	24	1	2	1	G4P1L1A2	8+4	1	20	2	0	0	1	0	1
	37	21	2	1	1	PRIMI	9+3	1	25	2	0	0	1	0	2
	38	31	1	1	2	G5P3L2A1	8+2	1	25	2	0	0	1	0	1
	39	30	2	1	1	G3P1L1A1	10	1	20	2	0	0	1	0	1
	40	27	2	1	0	G2P1L1	9+2	1	20	2	0	0	1	0	2